Chemical Library

Fourteenth Annual Observance National Pharmacy Week, October 16–22, 1938. See President's Letter and Bulletin Printed in This Number.

Vol. XXVII, No. 9 SEPTEMBER, 1938

JOURNAL OF THE AMERICAN PHARMACEUTICAL ASSOCIATION

TRADE MARK

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THE 87th ANNUAL MEETING OF THE AMERICAN PHARMACEUTICAL ASSOCIATION WILL BE HELD IN ATLANTA, GA., AUGUST, 1939.

The 1939 Meetings of the American Association of Colleges of Pharmacy, the National Association of Boards of Pharmacy, Conference of Pharmaceutical Association Secretaries, of the Pharmaceutical Law Enforcement Officials, National Conference of Pharmaceutical Research and the Plant Science Seminar will also be held in Atlanta, Ga.

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FAIRCHILD BROS. & FOSTER

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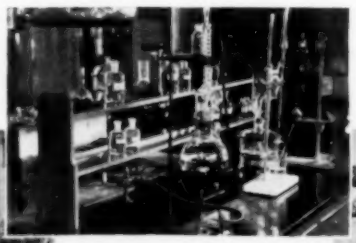
Holadin is also put up in capsules of 3 and 5 grains each.

DURING the summer months outdoor activities cause many minor injuries requiring first aid treatment. MERCUROCHROME, H.W. & D., (dibrom-oxymercuri-fluorescein-sodium) supplies your antiseptic needs. It is antiseptic, non-irritating and non-toxic in wounds. It has a background of eighteen years' medical acceptance.

A Mercurochrome display now will suggest the need of an extra supply for first aid kits or camp medicine chests. It will also be a reminder of the seasonal need of other first aid supplies.

An attractive display card will be sent to druggists on request.



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HYNSON, WESTCOTT & DUNNING, INC.

Baltimore, Maryland

THE WHITE HOUSE
WASHINGTON

Hyde Park, New York
September 8, 1938

My dear Dr. Lascoff:

I commend the observance of "National Pharmacy Week" in its purpose to stimulate greater health-consciousness among the people through cooperation with dependable druggists.

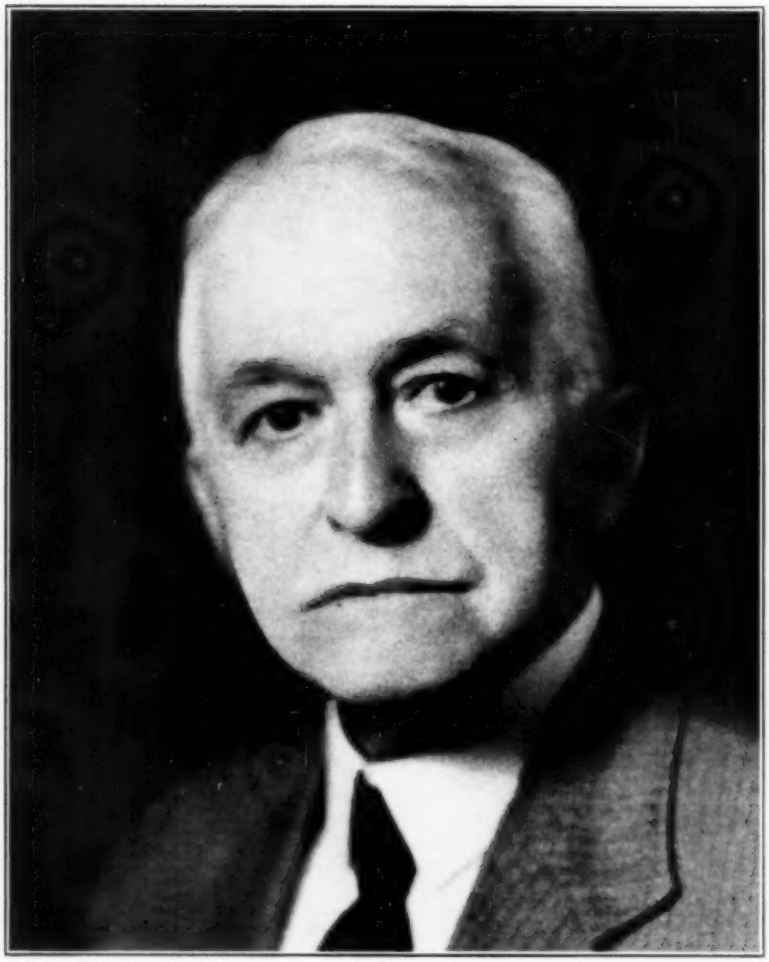
The pharmaceutical profession has an opportunity and a responsibility for constructive leadership in promoting the highest ethical standards - standards which make service the yardstick of success and confidence the guiding influence of the public in their pursuit of health.

I bespeak success for "National Pharmacy Week".

Very sincerely yours,

Franklin D. Roosevelt

Dr. J. Leon Lascoff,
President,
American Pharmaceutical Association,
1209 Lexington Avenue,
New York, N. Y.



EUGENE GUSTAVE EBERLE.

Member, 1896; Chairman, Section on Education and Legislation, 1901–1902; Secretary, Section on Commercial Interests, 1901–1902; Second Vice-President, 1902–1903; Secretary, Section on Historical Pharmacy, 1906–1909; First Vice-President, 1908–1909; Chairman, Section on Historical Pharmacy, 1909–1911; President (Boston meeting), 1910–1911; Chairman of the Council, 1911–1916; Editor of the JOURNAL, 1915–1938; Life Member, 1921; Remington Medalist, 1932; Editor Emeritus, 1938; Historian, 1915–

JOURNAL OF THE AMERICAN PHARMACEUTICAL ASSOCIATION

VOL. XXVII SEPTEMBER, 1938 No. 9

RETIREMENT OF EDITOR EBERLE.

At the Minneapolis meeting, Dr. Eberle submitted his resignation as Editor of the JOURNAL and was elected Editor of the JOURNAL, Emeritus, in which capacity he will be available for advice and guidance. Arrangements were made for Dr. Eberle to give his attention so far as his strength will permit, to the valuable historical material which the ASSOCIATION has collected during its eighty-seven years of existence and to assist in the Library and the Museum.

The ASSOCIATION attempted to express its appreciation of the fine personality and remarkable services of Dr. Eberle and also its good wishes to him in the following resolution:

"*Resolved*, that the AMERICAN PHARMACEUTICAL ASSOCIATION hereby expresses its sense of deep personal regret because of the enforced retirement, due to continual illhealth, of their esteemed colleague, Dr. Eugene G. Eberle, as Editor of the ASSOCIATION'S official JOURNAL.

"From the very beginning of his membership, Dr. Eberle has been one of the most active and faithful members in the ASSOCIATION. By his contribution of numerous valuable papers to its proceedings, by the efficient discharge of the duties attached to various Section Offices, which he has from time to time occupied, by his able administration of his office as President of the ASSOCIATION, and by his twenty-two years of faithful and able service as Editor of the JOURNAL, during which period it has come to be regarded as one of the leading publications of its kind in the world —by these and numerous other activities he has conferred great and lasting benefits upon the AMERICAN PHARMACEUTICAL ASSOCIATION and upon the profession it aims to represent.

"For his generous gifts to the Library and to the Historical and other collections; for his faithful devotion to duty in the various activities entrusted to him, and for his constant and unwearied promotion of the welfare of our Society, we shall always be profoundly grateful.

"Because of his unfailing courtesy, his constant and thoughtful regard for the opinions and feelings of others, and of his other splendid qualities of manhood, we,

his colleagues, who have so long enjoyed his fellowship in our official body, will always hold him in kindly remembrance.

"In releasing him from his position as Editor of the JOURNAL, it is the earnest hope of the members of the ASSOCIATION that by reason of his lessened labor and responsibilities he may be speedily restored to his accustomed health, and that he may be spared for many years of useful service as Editor Emeritus and as Historian of the ASSOCIATION and Curator of its Historical and other collections."

The AMERICAN PHARMACEUTICAL ASSOCIATION has been rich in the character of those who have served it in an official capacity and in the quality of the service that they have given to the ASSOCIATION and through it to the profession. E. G. Eberle has earned a high place in this distinguished group and at the same time the esteem and affection of the thousands whom he has earnestly striven to serve. That he may long enjoy the relief which he has so fully deserved is the sincere hope of his many friends and admirers.—E. F. K.

TO E. G. EBERLE.

A man is he to all his friends most dear,
And much esteemed for service, long and great,
To Pharmacy. A modest man, sincere
And true, whose virtues all might emulate.

A scholar, too, well-versed in literary art,
With wisdom to discern the truth, detect
The false, and thus to choose the better part
And merit admiration and respect.

A scientist with knowledge, broad and deep,
Of Chemistry and pharmaceutic lore,
Yet able all the while to learn and keep
In mind advances new with what has gone before.

A kindly man, most tolerant of those
Who hold to views of opposite belief;
An earnest and a faithful man, from whose
Long labor now there comes well-earned relief.

Now comes the time when leisure may be found
For pleasure which his active life deprived.
With health restored, both mind and body survived,
"The best of life" for him has now arrived.

WAYLAND D. WILCOX.

EDITORIAL

E. G. EBERLE, EDITOR EMERITUS. 2215 Constitution Ave., WASHINGTON, D. C.

THE MINNEAPOLIS MEETING.

THE PHARMACISTS of the Northwest may well take pride in the success of the 86th annual meeting in attendance, in interest, in the work accomplished and in the splendid entertainment provided for their visitors. Even the weather man coöperated in making this meeting a notable event.

The program of the annual meetings of the AMERICAN PHARMACEUTICAL ASSOCIATION and the related organizations that meet at the same time and place with it, is necessarily crowded and somewhat complicated due to the great amount of business that must be considered and disposed of during about ten days. The compensating advantages of this arrangement are that time and expense are saved, that the various divisions of pharmacy are brought into close personal contact with each other at least once in each year, that the views of these divisions on any matter of importance can be exchanged and that the decisions reached represent the conclusions of representatives of the entire profession. The large majority of the states, the colleges and the boards of pharmacy were represented. The attendance at the various meetings and the interest shown were very encouraging.

The profession now faces as many if not more problems and developments of pressing importance than at any time in the past. It is impossible to consider all of them in this brief review and, therefore, only the most important of these matters will be mentioned.

A national health program, whether it be known as socialized medicine or by some other name, and what effect such a program may have on pharmacy, was the outstanding topic. It came before the convention several times and from several points of view. The ASSOCIATION stated its position clearly in a resolution which recognizes that providing adequate medical care is a definite obligation of society; which stated that drugs, medicines and medical supplies are an indispensable phase of adequate medical care; which pledges its coöperation in developing suitable plans for using the existing agencies now furnishing medical services in any program which may be developed; and which urges that in any such program the free choice of physician, dentist, pharmacist and nurse by the patient be retained as a basic principle. In other words, a coördinated national health program to furnish adequate medical care is recognized as necessary; existing agencies now furnishing health services should be employed in this program; and the present right of patients to choose the physicians, dentists, pharmacists and nurses which shall serve them, should be retained.

The Study of Medical and Preventive Medical Needs now being conducted by state and county medical societies also came in for considerable discussion. This study is intended to develop dependable information about how adequate medical care is and what is necessary to improve the service. Dr. R. G. Leland, Director, Bureau of Medical Economics of the American Medical Association, spoke about the study at length. The ASSOCIATION pledged its continued support in this study; urged the pharmacists of the country to furnish the information requested of them on Questionnaire No. 9 and urged the state and local associations to coöperate in this

effort. The response made by many pharmacists and their clear understanding of the present situation were commented upon favorably. Pharmacists are very close to the people and are therefore competent to reflect public opinion about the adequacy of medical care.

The Federal Food, Drug and Cosmetic Act and the Federal Trade Commission Act, and the steps which the states should take in bringing their legislation into harmony with the national laws were other subjects of great interest. Almost an entire session of the House of Delegates was devoted to its discussion. The prevailing opinion was that the state acts should be revised or amended promptly.

A Committee consisting of R. P. Fischelis, R. L. Swain, C. Leonard O'Connell and A. L. I. Winne was appointed to draft a suggested procedure covering the drug and cosmetic features of the national laws, which will be submitted to the state associations early in the fall and in time for consideration prior to the sessions of the state legislatures, which will be held in a large majority of the states during 1939. The ASSOCIATION also adopted a resolution expressing gratification that the national laws were enacted, pledging its support in their effective enforcement and urging the state associations to so amend their laws as to give intra-state effort to those provisions of the national laws which are considered to be feasible and applicable to the needs of the states. During the entire discussion of these acts, emphasis was placed on their public health value and on the duty of the pharmacists to support measures intended to protect the public welfare.

The modernization of the state pharmacy laws was an important topic. The Committee on the Modernization of Pharmacy Laws submitted a report at the New York meeting in 1937, which had drawn a broad foundation for bringing these laws into harmony with the present-day needs of the public as well as of the pharmacists, and projected some unusual developments in the plans to so amend these laws as to emphasize the interest which the public should take in their enforcement. The report which the Committee submitted this year was an extension of the previous report. It dealt first with the importance of similarity in names and terms in state laws and of accord between such names and terms and those employed in Federal acts affecting pharmacy. For instance, it is important that the term "drug" should mean the same in the state pharmacy acts as it does in the Federal Food, Drug and Cosmetic Act and the Federal Trade Commission Act. The report summarized the variations in state acts, particularly in the substances covered under the so-called exemption clauses. The Committee regretted its inability to submit a model draft of a state pharmacy law for discussion at the meeting and expressed the hope that such a draft could be made available to state associations in October or November. The committee requested that the secretaries of state boards of pharmacy be made auxiliary members in order to expedite the work, and submitted two recommendations which were supported by resolutions adopted by the ASSOCIATION. The first favored giving boards of pharmacy the power to stipulate the minimum of professional and technical equipment which must be at all times available in every pharmacy, and the second favored legislation requiring manufacturers of drugs and medicines to operate under annual permits issued by the State Board of Pharmacy. Legislation covering both recommendations is now in successful operation in several states and is serving a good purpose. Copies of these laws are available.

The ASSOCIATION took a strong position in support of the American Council on Pharmaceutical Education and the work which the Council is doing in developing satisfactory standards for the accreditment of schools and colleges of pharmacy and in applying these standards to such of the schools and colleges as request accreditment with the object of issuing a list of accredited institutions in the fall of 1939. The Council represents the A. PH. A., the N. A. B. P. and the A. A. C. P., and has an advisory member from the American Council on Education. This is an effort to place pharmaceutical education on a sound basis and it is noteworthy that the profession itself has undertaken the work through its own personnel and finances. In the effective discharge of the important duties entrusted to it, the Council deserves the support of every pharmacist, every professional association, every teaching institution and every board of pharmacy in the United States.

Attention was given to coördinating and extending the work now being carried on to strengthen the relations between pharmacists and the members of the other public health professions and to promote the use of official drugs and preparations. A meeting of the members of the committees which the state associations have appointed for these purposes was held for the first time. There was a representative attendance and arrangements were made for an organization through which these committees can coöperate by an interchange of information and suggestions. The plans and materials used in each state will be brought to the attention of other states, and will also be preserved in the INSTITUTE OF PHARMACY for future reference. The Committee on Dental Pharmacy submitted a National Dental Program which will be followed in contacting the dentists.

The name of the Committee on the Study of Pharmacy was changed to that of Committee on Social and Economic Relations in order that the ASSOCIATION can give consideration through the Committee to employer-employee relations, necessary services in the field of health care, and other matters involving the relations of pharmacy to the national social and economic structure.

The participation of pharmacists and the coöperation of the state and local associations in the Venereal Disease Campaign was given consideration in several groups. Since the ASSOCIATION had expressed its position in reference to the campaign at the New York meeting by resolutions, no official action was taken at Minneapolis.

Hospital pharmacy came very much to the front at the meeting. The Subsection on Hospital Pharmacy held two sessions and other group meetings were held. Arrangements were completed to survey the pharmacies in the hospitals of the country and to organize hospital pharmacists in the A. PH. A. through local units. The ASSOCIATION will coöperate closely with the national hospital associations in these and other efforts to improve pharmaceutical services in hospitals and the status of hospital pharmacists. Unfortunately, Dr. Malcolm T. MacEachern, Associate Director of the American College of Surgeons, who was scheduled to address the second General Session on "Hospital Pharmacy," could not attend but sent a very encouraging message pledging the continued coöperation of the College. In his absence, Chairman Mordell, of the Sub-section on Hospital Pharmacy, gave a splendid address outlining the work of his group and the plans for the future.

The Committee on National Formulary held a two-day session during which plans were made to complete all of the proposed changes in N. F. VI during the coming year and to turn over a completed manuscript to the new Committee on National Formulary when it is elected at the 1939 meeting. Arrangements were also made to complete the monographs dealing with the new diagnostic and clinical reagents in order that this important new section of the National Formulary may be given general study and trial before its inclusion in the seventh edition.

The Committee on Pharmaceutical Syllabus also held several sessions, during which it was decided not to issue a revision of the publication at an early date, but rather to give more time and study to the revision with the view to making the Syllabus of greater usefulness not only to the boards and colleges but also to the American Council on Pharmaceutical Education.

The Plant Science Seminar met the week preceding and had a fine program and a good attendance. Good work was done by the Conference of Secretaries and the Conference of Law Enforcement Officials. The Conference on Pharmaceutical Research held its usual sessions on the Saturday preceding and decided to find a time and place for its meetings during the ASSOCIATION week, if possible.

Reference has been made to two addresses scheduled during the meeting. Several others of importance were delivered. Outstanding among them was the address of President Byrd of the University of Maryland, who spoke on "Public Support for Professional Education" and how to interest taxpayers in the importance of professional education.

The Council of the A. PH. A. dealt with a large volume of business during the week. Special attention was given to a reorganization of the publication program of the ASSOCIATION, to the arrangements for the annual meetings, to improving the observance of Pharmacy Week, to perfecting the plans for the A. PH. A. Laboratory, to awards from the Research Funds, and to plans for awarding the Ebert and Kilmer Prizes.

The Ebert Prize was awarded to Frederick F. Johnson for his paper presented at the New York meeting on "Solubility and Hydrogen-Ion Concentration of Quinine Salts."

The resolutions adopted during the meeting were of unusual importance and are printed in this issue. They should be carefully studied and actively supported.

The names of the officers elected during the meeting and those nominated for election by mail ballot are also printed in this issue. The election of the officers who will govern the ASSOCIATION is a duty of vital importance to which the members are urged to give prompt and careful attention when the ballots reach them in October.

The ASSOCIATION received two new funds during the meeting—a further payment of about $1800.00 from the estate of the late Franklin M. Apple and $2000.00 for the George and Lillian Judisch Memorial Fund, the income from the latter to be used to promote professional Pharmacy.

Altogether, this was a successful meeting and the work completed, continued and begun should have a real value for Pharmacy in our country.—E. F. K.

OFFICERS AND NOMINEES.

The following were nominated during the recent Minneapolis meeting for the respective officers named:

PRESIDENT.

A. G. DuMez, *Dean*, College of Pharmacy, University of Maryland.
A. F. Marquier, *Retail Pharmacist*, Newark, N. J.
Oscar Rennebohm, *Retail Pharmacist*, Madison, Wis.

FIRST VICE-PRESIDENT.

C. H. Evans, *Retail Pharmacist*, Warrenton, Ga.
F. O. Taylor, *Chief Chemist*, Parke, Davis & Co., Detroit, Mich.
W. J. Teeters, *Dean Emeritus*, Iowa City, Iowa.

SECOND VICE-PRESIDENT.

Frederick J. Cermak, *Retail Pharmacist*, Cleveland, O.
C. O. Lee, *Professor*, College of Pharmacy, Purdue University, La Fayette, Ind.
E. V. Lynn, *Professor*, Massachusetts College of Pharmacy, Boston, Mass.

MEMBERS OF THE COUNCIL.

H. C. Christensen, *Secretary*, National Association Boards of Pharmacy, Chicago, Ill.; R. P. Fischelis, *Board Member*, Trenton, N. J.; Ernest Little, *Dean*, College of Pharmacy, Newark, N. J.; A. L. I. Winne, *Board Member*, Richmond, Va.; C. B. Jordan, *Dean*, College of Pharmacy, Purdue University, La Fayette, Ind.; R. A. Lyman, *Dean*, College of Pharmacy, University of Nebraska, Lincoln, Nebr.; W. Mac Childs, *Retail Pharmacist*, Eldorado, Kans.; George A. Moulton, *Board Member*, Peterborough, N. H.; W. F. Sudro, *Dean*, College of Pharmacy, Fargo, N. Dak.

The names of these candidates will be submitted by mail about October first to the members of the Association, with a ballot, for the election of the President, the First Vice-President, the Second Vice-President, all to serve one year, and three Members of the Council, to serve three years. Those elected will be installed during the closing session of the 1939 meeting which will be held in Atlanta, Ga.

The officers elected by mail ballot last fall and installed during the Minneapolis meeting are: J. Leon Lascoff, New York, N. Y., *President;* A. O. Mickelsen, Portland, Ore., *First Vice-President;* G. A. Moulton, Peterborough, N. H., *Second Vice-President;* Roy B. Cook, Charleston, W. Va., Glenn L. Jenkins, Minneapolis, Minn., and R. L. Swain, Baltimore, Md., *Members of the Council.*

During the Minneapolis meeting the following officers were elected to serve during the year 1938–1939: W. C. Anderson, Brooklyn, N. Y., *Honorary President;* E. F. Kelly, Washington, D. C., *Secretary;* C. W. Holton, Essex Fells, N. J., *Treasurer;* C. H. Rogers, Minneapolis, Minn., *Chairman*, and R. A. Kuever, Iowa City, Iowa, *Vice-Chairman of the House of Delegates.*

A PHARMACY WEEK MESSAGE.

As president of the AMERICAN PHARMACEUTICAL ASSOCIATION I am calling upon the pharmacists of this country to whole-heartedly coöperate in making National Pharmacy Week a splendid success. This great effort in behalf of professional Pharmacy will be observed from October 16th to October 22nd, and I am particularly interested in this observance.

National Pharmacy Week was established fourteen years ago for the specific purpose of uniting pharmacists in a special effort directing attention to the great public health significance of the retail drug store. As its founder, Dr. Ruth, so well said, "Public health must be the key-note." It was felt that such a plan would contribute greatly to giving Pharmacy its rightful place in public esteem. It was believed that Pharmacy would gain much from having the public regard it from the standpoint of its intrinsic professional service and of the importance of the drug store as a public health station.

Few callings touch the public welfare so vitally as Pharmacy. The pharmacist is called upon, day and night, to make available the drugs, medicines and medical supplies upon which public health so largely depends. Many of these products are extremely dangerous and must be dispensed by competent and skilful hands, and with dependable advice.

On this account the pharmacist is required to undergo a stringent period of professional training and to satisfy the state that he is competent to serve the public adequately and safely. Every time a pharmacist is called upon to fill a prescription he deals in a very vital way with health and happiness. Events of real human interest are routine affairs to pharmacists as they pursue their daily work. All of this affords a dramatic background from which to make the drug store stand out as something fine and something essentially different from other institutions on the streets of our towns and cities.

I believe that National Pharmacy Week is sound in principle and that nothing but good can come from calling attention to the professional function and service of Pharmacy. It is, perhaps, too much to ask every pharmacist to emphasize the professional aspect of his store at all times but certainly it is not too much to ask that he devote one week out of a year to a special effort to present Pharmacy to the public in the most effective manner.

If National Pharmacy Week has failed to serve the high purpose for which it was intended it is because the pharmacists of the country have not coöperated in making it succeed. It is to be forever kept in mind that the public appreciation of Pharmacy can never rise higher than our own, and that our failure to reflect its professional character is certain to result in failure on the part of the public to value Pharmacy as its true worth.

It is because I think National Pharmacy Week is sound in principle and in our interest as well as the public that I very earnestly call upon all pharmacists to recognize their responsibility in the matter and to do everything possible to make National Pharmacy Week serve its purpose. Window displays, interior displays, public addresses, radio addresses, newspaper articles, all aimed at the essential service which Pharmacy renders, are bound to create a sounder appreciation on the part of the public and, in due course, to give Pharmacy that place in public estimation which its responsibility so clearly warrants.

If National Pharmacy Week falls short of its objective, it will be due to no other cause than that we ourselves failed to rise to the occasion.—J. LEON LASCOFF.

NATIONAL PHARMACY WEEK COMMITTEE
2215 CONSTITUTION AVE., WASHINGTON, D. C.

FOURTEENTH ANNUAL OBSERVANCE NATIONAL PHARMACY WEEK, OCTOBER 16–22, 1938.

Preparations are now under way for the 14th annual observance of National Pharmacy Week. The success of this splendid movement, founded by the late Dr. Robert J. Ruth, depends in a large measure upon the professional activities of the retail pharmacists and all are urged to take an active part.

Pharmacy, as a profession, is judged mainly by the services and appearance of the retail drug store. Therefore, Pharmacy Week offers an excellent opportunity to focus public attention on the professional activities carried on in the retail drug stores of the nation and in other branches of Pharmacy.

Arrange an Interesting Program.—The following suggestions are made by the AMERICAN PHARMACEUTICAL ASSOCIATION which sponsors Pharmacy Week in coöperation with the National state and local pharmaceutical groups.

(*a*) Arrange for professional window displays. A survey of the winning displays in recent years shows that effective displays should have a main theme or subject and should not contain so much material as to confuse those who see it. Make the message clear and easily understood.

(*b*) Arrange for several interior professional displays. These displays should tie in with the window display.

(*c*) Arrange for distribution of interesting messages about Pharmacy Week, including notes on the professional window and other displays, in the form of educational package and enclosed inserts.

(*d*) Arrange for mailing well-prepared professional communications about Pharmacy Week to members of the allied professions and to include in them an invitation to inspect the Pharmacy Week displays.

(*e*) Arrange for appropriate articles and editorials in local newspapers and other publications.

(*f*) Arrange for one or more talks before local and particularly civic organizations and for radio broadcasts over local stations.

(*g*) It is hoped that Colleges and Pharmaceutical Associations will again arrange suitable Pharmacy Week displays and other activities intended to draw attention to this observance.

(*h*) In case your Association or College has a program during this week, arrange to be in attendance and to interest as many people as possible in the program.

A series of Pharmacy Week Articles has been prepared for use in connection with the above suggestions. The titles of these articles are listed on page 736.

It is difficult to prepare an interesting professional window display and program in a short period of time. *BEGIN NOW!* Talk the matter over in detail with your associates and assign each a definite thing to do.

Pharmacy Week National Window Display Prize and Honorable Mention Certificates.—As in former years, the Robert J. Ruth Memorial Trophy consisting of a silver loving cup donated by the Federal Wholesale Druggists' Association, will become the permanent possession of the winner in the National Pharmacy Week Window Display Contest. In addition to this prize, there will be awarded jointly by the AMERICAN PHARMACEUTICAL ASSOCIATION and the National Association of Retail Druggists to the ten next best window displays, Honorable Mention Certificates which when framed will prove to be interesting certificates for the interior of the store as well as for professional window displays. Entries in the National Contest are limited to the photographs of the winning displays in the state contests.

Rules of the National Contest.—(1) Photographs of professional window displays must be submitted to the Secretary of the State Pharmaceutical Association on or before November 15th, in order that the winner may be judged and entered in the National Contest.

(2) Photographs as submitted in former years will be ineligible.

(3) Photographs should be accompanied with a brief descriptive text together with letter of transmittal.

(4) Photographs should be 8 x 10 inches in size, or some other suitable size, so that the judges will be enabled to study details of the display.

State, County and Local Pharmacy Week Prizes.—Numerous other prizes in the form of silver loving cups, mortars and pestles, etc., will be awarded by state, county and local pharmaceutical organizations. The Secretaries of the State Associations can furnish information about such contests and the awards.

Pharmacy Week Awards for Associations and Colleges.—The AMERICAN PHARMACEUTICAL ASSOCIATION will present the state, county or local pharmaceutical organization a Pharmacy Week award for the best professional window display as prepared and featured by the organization. The award last year was won by the Philadelphia Association of Retail Druggists. Another award will be presented to the College or School of Pharmacy which prepares and features the best professional window display. The award last year was won by the Temple University School of Pharmacy. Photographs should reach the National Pharmacy Week Committee before December 15th.

National Pharmacy Week Radio Broadcasts.—Arrangements have been made for addresses by representatives of the AMERICAN PHARMACEUTICAL ASSOCIATION over the national broadcasting networks. Watch for announcements of the date and time of these broadcasts.

Pharmacy Week Articles.—The human interest-appeal Pharmacy Week articles have proved to be a very helpful feature of Pharmacy Week observance. Thousands of copies were distributed last year and the series has been revised with the hope that a larger number will be used this year.

Please check the following list and mail your request for copies promptly to the above Committee. Copies are available, as follows: 3 copies free of charge; any 15 copies, 50¢; entire series $1.00.

No.

1 Medicine Obtained from Animals
2 The Service of Pharmacy
3 Medicine Made from Bacteria
4 The Modern Medicine Man
5 The Romance of Foxglove
6 The Value of Research
7 Famous Discoveries by Famous Pharmacists
8 The Coal Tar Rainbow
9 Root Diggers' Corner
10 The Drug Store and the Community
11 The Value of Pharmacy to the Public
12 Drugs of the Scriptures
13 Drugs of the North American Indians
14 The Origin and Significance of the Pharmacists' Show Globes
15 Mankind and Medicine
16 Yes Indeed! I Am Mighty Glad to Be a Pharmacist
17 The Pharmacist and the Public
18 The Evolution of Drugs
19 Drugs Old and New
20 Mandragora, a Sleeping Draught from Ancient Times
21 The Pharmacist as a Purveyor of Drugs
22 The Story of Insulin
23 The Apothecary in Literature
24 The Geography of Medicines
25 Jungle Memories of Drug Investigations
26 Hospital Pharmacy

NAME.....

STREET & NUMBER.....

CITY & STATE.....

AMOUNT ENCLOSED.....DATE.....

RESOLUTIONS AND RECOMMENDATIONS ADOPTED BY THE AMERICAN PHARMACEUTICAL ASSOCIATION AT ITS EIGHTY-SIXTH ANNUAL MEETING IN MINNEAPOLIS, MINN., AUGUST 22–27, 1938, UPON RECOMMENDATION OF THE HOUSE OF DELEGATES THROUGH THE COMMITTEE ON RESOLUTIONS.

The AMERICAN PHARMACEUTICAL ASSOCIATION expresses its grateful appreciation for the valuable contributions made to the ASSOCIATION, and to American Pharmacy, by the prudent but progressive administration of its affairs by President Gathercoal, and it commends and praises the comprehensive survey of the ASSOCIATION'S many useful activities in his admirable presidential address.

No. 1. Resolved, that the AMERICAN PHARMACEUTICAL ASSOCIATION expresses its deep gratification that the Federal Food, Drug and Cosmetic Act and the Federal Trade Commission Act were enacted during the recent session of the Congress, pledges its support toward the effective enforcement of these Acts and urges the state pharmaceutical associations to give prompt study to these Acts in order that the state laws may be revised or amended to give intra-state effect to those provisions of the Acts which are considered to be feasible and applicable to the needs of the states.

No. 2. WHEREAS, the profession of Pharmacy is now engaged through an agency which it established for that purpose, in developing acceptable standards for the accreditment of schools and colleges of pharmacy and a list of the schools and colleges which comply with these standards, as a further protection of the public welfare and of Pharmacy's professional standing,

Resolved, that the AMERICAN PHARMACEUTICAL ASSOCIATION pledges its continued support to the American Council on Pharmaceutical Education in the effective discharge of the very important duties which have been entrusted to the Council.

No. 3. Resolved, that the AMERICAN PHARMACEUTICAL ASSOCIATION expresses its deep concern over the provisions of the Federal and state narcotic acts which permit the unregulated and promiscuous retail distribution of exempt narcotics, and

Resolved Further, that the views of the ASSOCIATION be made known to the Federal Commissioner of Narcotics with the urgent request that further study be given to national legislation which will more adequately control the manufacture of exempt narcotics.

No. 4. Resolved, that the AMERICAN PHARMACEUTICAL ASSOCIATION notes with great pleasure the many programs being carried on in every state in the country to promote closer relations between the members of the public health professions and pledges its support to this movement, and

Resolved Further, that the committees appointed for this purpose by the state associations be complimented on the very effective work that they are doing.

No. 5. Resolved, that in view of recent public health developments, the AMERICAN PHARMACEUTICAL ASSOCIATION again urges that pharmacists be appointed to membership on the state and local boards of health and requests the state pharmaceutical associations to take the necessary steps to bring about such appointments.

No. 6. Resolved, that the Federal Commissioner of Narcotics and his associates be commended for their effective services in the enforcement of the Harrison Act and for their efforts to secure coöperation from other countries in the control of narcotic and other dangerous drugs.

No. 7. Resolved, that the AMERICAN PHARMACEUTICAL ASSOCIATION express its thanks to A. L. I. Winne, Chairman of the House of Delegates, for his informative and fruitful address, and especially for the keen analysis of the source of the membership, the functions and the procedure of the House of Delegates.

No. 8. Resolved, that a committee be appointed to study the By-Laws covering membership in the House of Delegates, to determine whether they should be amended so as to accord more equitable voting power as between large and small groups now given voting power in this body.

No. 9. Resolved, that the AMERICAN PHARMACEUTICAL ASSOCIATION opposes the sale of obscene literature, and that it calls upon retail pharmacists handling magazines and publications to exercise necessary censorship and care over the type of publications distributed.

No. 10. WHEREAS, ethyl alcohol is a necessary and indispensable ingredient either as a solvent or as a preservative or both, of many important drugs, medicines and medical supplies,

Resolved, that the AMERICAN PHARMACEUTICAL ASSOCIATION urges the Federal and state governments to remove any excise tax from ethyl alcohol used in bona fide medicinal substances with such safeguards and penalties against abuse as may be necessary, in order that the cost of these substances to the sick may be more reasonable.

No. 11. Resolved, that the AMERICAN PHARMACEUTICAL ASSOCIATION continue to coöperate, and that it urges the state and local pharmaceutical associations to coöperate, in the Study of Medical and Preventive Medical Needs now being conducted by the state and local medical societies, in order that the information sought may be comprehensive and may be made available promptly.

Resolved Further, that the pharmacists of the country be requested to furnish the data sought from them in this connection.

No. 12. Resolved, that the AMERICAN PHARMACEUTICAL ASSOCIATION expresses its approval of all efforts being made to better pharmaceutical practice, and to this end urges all state pharmaceutical associations and boards of pharmacy to stipulate the minimum of professional and technical equipment which must be at all times in possession of every place conducted as a pharmacy.

No. 13. Resolved, that the AMERICAN PHARMACEUTICAL ASSOCIATION again expresses its deep interest in all matters having to do with the standards of drugs and medicines, and to the improvement of the conditions surrounding their manufacture and production, and to this end records its approval of those state laws which require all manufacturers of these highly essential public health commodities to operate under permits issued by the Board of Pharmacy, and

Resolved Further, that the ASSOCIATION urges the amendment of state pharmacy acts so as to make this type of regulation and control legally possible, and,

Resolved Further, that the ASSOCIATION believes it is highly desirable that a uniform state law regulating the conditions of manufacture of medicinal products be drawn up for the guidance of the various states.

No. 14. Resolved, that the AMERICAN PHARMACEUTICAL ASSOCIATION expresses its gratification at the increased interest in pharmaceutical legislation now being manifested throughout the country, and that it pledges its active aid and coöperation to all efforts now being made in the various states to bring state pharmacy acts into conformity with pharmaceutical education and the needs of public health.

No. 15. Resolved, that the AMERICAN PHARMACEUTICAL ASSOCIATION expresses its profound appreciation of the scholarly, frank and stimulating address delivered before this convention by Dr. H. C. Byrd, President of the University of Maryland, and that copies of the address be sent to the Presidents of Universities and Colleges having Schools of Pharmacy, to the Deans of these Schools of Pharmacy, members of the State Boards of Pharmacy, Secretaries of State Pharmaceutical Associations and to the pharmaceutical press.

No. 16. (See page 727.)

No. 17. WHEREAS, the duties of the Committee on the Study of Pharmacy of the AMERICAN PHARMACEUTICAL ASSOCIATION have been enlarged to include consideration of such vital matters as employer-employee relations and governmental participation in supplying necessary services in the field of health care, as well as other matters involving the relation of Pharmacy to our social and economic structure,

Resolved, that the name of this committee be changed to the Committee on Social and Economic Relations.

No. 18. WHEREAS, World's Fairs are scheduled to be held in New York and San Francisco during 1939, and

WHEREAS, Exhibits of the progress and scientific achievements of Pharmacy constitute an important part of such international expositions,

Resolved, that the AMERICAN PHARMACEUTICAL ASSOCIATION hereby voices its disapproval of the use of the historical and scientific background of professional Pharmacy in association with commercial displays of proprietary medicines offered to the public for self-medication.

No. 19. WHEREAS, the necessity for making adequate medical care available to citizens in all income groups is recognized as a definite obligation of society, and

WHEREAS, the furnishing of drugs, medicines and medical supplies constitutes an indispensable phase of adequate medical care,

Resolved:

1. That the AMERICAN PHARMACEUTICAL ASSOCIATION expresses its profound interest in all plans proposed for extending medical care,
2. That the ASSOCIATION pledges its coöperation in devising suitable plans for the ultilization of existing agencies now providing medical services, and
3. That the ASSOCIATION strongly urges the retention of free choice of physician, dentist, pharmacist and nurse, by the patient, as an essential feature in whatever system may be adopted.

No. 20. Resolved, that the AMERICAN PHARMACEUTICAL ASSOCIATION hereby extends sincere appreciation to Charles H. Rogers, Chairman of the General Convention Committee, Walter Fields, Chairman of the Entertainment Committee, Charles V. Netz, Treasurer, Mrs. Keith Keller, Chairwoman of the Ladies' Committee, and all others who have contributed to the enjoyment and comfort of our delegates, for the most efficient and hospitable handling of accommodations and social events for the 86th annual meeting, and

Resolved Further, that the ASSOCIATION commends particularly the good taste and the high standard of excellence of the entertainment provided.

U. S. CIVIL SERVICE EXAMINATIONS.

The Civil Service Commission announced on August 22nd, examinations for Assistant Investigator (Pharmacy) at $2600.00 a year. "To inspect books and stocks of manufacturers and druggists, and to investigate cases arising from illegal diversion of narcotic drugs from legitimate channels."

The examinations were scheduled in various sections of the country and application forms were available from the Secretary, Board of U. S. Civil Service Examiners at any first-class postoffice. Applications were required to be on file with the U. S. Civil Service Commission by not later than September 15th, for the western states and by not later than September 12th, for other states.

Applicants must be between 21 and 45 years of age, must pass a rigid physical examination and a written examination covering a general investigation test and the theory and practice of Pharmacy. They must have successfully completed all of the requirements either for the degree of Bachelor of Pharmacy in a recognized School of Pharmacy or in a college or university of recognized standing, or the degree of Doctor of Medicine in a recognized medical school; or they must have registered as a pharmacist in a State, Territory or the District of Columbia. In addition, they must have had at least two years of practical experience as a pharmacist (subsequent to registration or completion of the pharmacal or medical education) in connection with the filling and compounding of physicians' prescriptions (or work of equivalent character) either in responsible charge of such work or under the supervision of a licensed pharmacist; or they must have had at least one year of major investigative experience.

SCIENTIFIC SECTION

BOARD OF REVIEW OF PAPERS.—*Chairman*, F. E. Bibbins; H. M. Burlage, W. G. Crockett, E. V. Lynn, C. O. Lee, L. W. Rising, L. W. Rowe, Heber W. Youngken, Ralph E. Terry, Carl J. Klemme.

A PHARMACOLOGICAL STUDY OF USTILAGO.*[1]

BY WILLIAM H. HUNT[2] AND MARVIN R. THOMPSON.[3]

Ustilago was defined in the United States Pharmacopœia of 1880 (1) as the spores of *Ustilago maydis*, which are parasitic on various parts of the corn plant. It appears as irregular, globose masses, sometimes 15 cm. thick, consisting of a blackish membrane inclosing innumerable brown-black, globular and nodular spores and possessing an unpleasant odor and taste.

This parasitic growth upon corn, commonly known in the United States as "smut," has doubtless appeared with the cultivation of maize from a very remote period, though the precise date of its earliest notice is difficult to ascertain from the literature.

A review of the literature, historical and otherwise, is presented and discussed in the original thesis.

Among the earlier investigators the work of the following merit mention in connection with the present investigation: Jussieu, Linnaeus, Leveille, Tulasne brothers, Waldheim, Wolf, Winter, Farlow, Prillieux and Spalding (2).

The exact time of the first chemical investigation of *Ustilago maydis* is obscure, but among the earlier investigators Cressler's (3) work appears to be among the first. Other investigators, such as Parsons (4), Rademaker (5), Rademaker and Fischer (6), Balch (7), Testoni (8), and Langecker (9), have also searched for active principles, which, from time to time, have been reported as alkaloidal. Recent investigations have shown that the active substance, if an alkaloid, cannot be demonstrated as such by the usual methods.

A review of the literature indicates that the use of this drug was very extensive during the period of 1875 to 1890. It was considered to be of sufficient merit to be included in the United States Pharmacopœia, Sixth Decennial Revision. However, it was deleted in the Seventh Decennial Revision. The deletion may be attributed to the conflicting reports which arose following numerous clinical, chemical and pharmacological investigations and a consequent lack of acceptable proof of value. The clinical evidence for its admission and deletion is clearly portrayed by Leonard (10), (11), Crist (12), Cooperiden (13), Goss (14), Vailliant (15), Hale (16), and Mitchell (17).

Bogdanovitch (18) reported that fluidextract of Jugoslavian *Ustilago maydis* possessed various properties, with which the present work agrees in part. The differences occur in the results obtained by the following methods of experimentation: the action upon the isolated rabbit intestine, and the effect upon the hypertensive action of epinephrine.

Dragisic and Varicak (19) have reported that Jugoslavian *Ustilago maydis* possesses an ergotamine-like principle. In this work we have been unable to confirm their results regarding this action. However, it may be possible that there is a pronounced difference in the nature of the drug from these widely separated sources.

Since the literature reveals many conflicting reports concerning the activity of *Ustilago maydis*, a qualitative pharmacodynamic investigation of the drug was initiated. This investi-

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* Presented before the Scientific Section, A. PH. A., New York meeting, 1937.

[1] From a Thesis submitted by William H. Hunt to the Faculty of the Graduate School of the University of Maryland in partial fulfilment of the requirements for the degree of Doctor of Philosophy, 1937.

[2] Pharmacologist, The Maltbie Chemical Co., Newark, N. J.

[3] Professor of Pharmacology, School of Pharmacy, Univ. of Maryland.

gation embraced studies upon certain functions and organs of the intact animal, as well as upon isolated organs, such as blood pressure, uterine experiments *in vivo* and *in vitro*, isolated intestine, perfusion of blood vessels, etc.

THE EFFECT OF USTILAGO ON THE BLOOD PRESSURE OF THE CAT.

Two hundred grams of ground, mixed, air-dried ripe and unripe drug were first macerated for eight hours and then percolated with 1000 cc. of 50 per cent alcohol until the drug appeared to be exhausted. The percolate at all times was kept in the refrigerator to prevent possible deterioration by light or heat. This percolate was finally adjusted by evaporation in a current of air, without heat, so that 1 cc. was equivalent to 1 Gm. of drug.

A non-pregnant female cat, weighing 2.7 Kg., was anesthetized by an intraperitoneal injection of sodium amytal, and prepared in the conventional manner for a blood pressure determination. The right femoral vein was exposed and canualized for the purpose of injecting the drug. After obtaining the control, 0.3 cc. of the percolate was injected into the femoral vein. A transitory fall of blood pressure was produced.

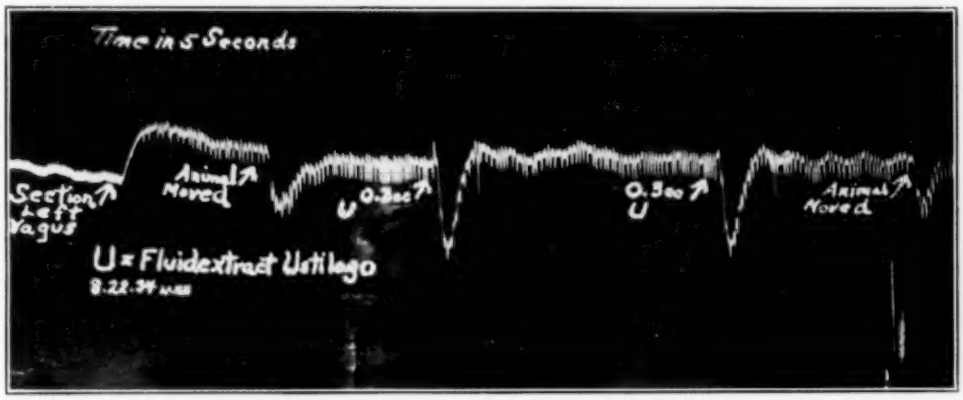

Fig. 1.

After sectioning the right vagus, a repetition of the same dose duplicated the preceding result. The left vagus was then sectioned, the results of which may be seen in Fig. 1. Following this procedure 0.3 cc. of drug was administered intravenously, producing a transitory effect similar to that noted before the section of the vagi. The dose was repeated to confirm the preceding result. Increased doses of the drug gave correspondingly greater depressor effects.

The above experiment having shown that the drug possessed a principle which produced a transitory depressor effect, it was decided to determine the action of the fluidextract upon the pressor effect produced by epinephrine.

A non-pregnant female cat, weighing 2.65 Kg., was anesthetized with ether and prepared in the same manner as the preceding experiment. Repeated doses of epinephrine hydrochloride solution were administered intravenously until consistent results were obtained. The employed doses of fluidextract of *Ustilago maydis* exerted no "ergot-like" influence on the pressor responses of epinephrine. In this experiment the vagi remained intact and again the depressor effect of the drug was clearly evident.

Having seen the results of the fluidextract of *Ustilago maydis* upon the blood pressure of the cat whose vagi remained intact, and in the case where the vagi were sectioned, it was decided to determine the effect of the fluidextract following the administration of atropine sulfate.

A non-pregnant female cat, weighing 2.62 Kg., was lightly anesthetized with sodium amytal and prepared in the manner of the preceding experiments. Following the intravenous administration of duplicate doses of epinephrine hydrochloride (1–50,000), 1 mg. per Kg. of atropine sulfate in saline was administered intravenously. After the blood pressure returned to a constant level, 1 cc. of epinephrine hydrochloride solution was administered intravenously until

consistent results were obtained. At this time 5 cc. of the fluidextract, used in the previous experiments, were injected intravenously. As may be seen in Fig. 2, a correspondingly greater and more prolonged depressor action was recorded. Two successive doses of epinephrine hydrochloride solution were then administered, producing the usual pressor responses. This confirmed the previous observation that the fluidextract produced no "ergot-like" influence on the action of epinephrine hydrochloride.

Since section of the vagi and the effect of atropine sulfate both inhibit vagal effects, it appears that the depressor effect produced by the fluidextract is the result of an action upon a site other than the parasympathetic innervation of the heart and arterial system. Since the parasympathetic nervous system, which when stimulated causes a dilatation of blood vessels, is depressed by the action of atropine sulfate, and since the prior administration of the fluidextract neither inhibits nor augments the subsequent action of epinephrine hydrochloride (showing no action upon the sympathetic innervation of the blood vessels) it may be concluded that the fluidextract probably causes its depressor effect by acting directly upon the blood vessels themselves. In support of this view, a carotid blood pressure experiment upon a 3.1 Kg. cat showed that ergotoxine, in dosage sufficient to produce a "reversal" of the effect of epinephrine, failed to influence the depressor action of the fluidextract.

In an effort to determine the nature of the principle responsible for the depressor activity, ripe and unripe drugs were thoroughly mixed and percolated with petroleum ether. After this extraction the marc was exhausted with a menstruum of 50 per cent alcohol. The petroleum-ether solution was allowed to evaporate until all traces of its odor were removed, after which the residue was taken up in 95 per cent alcohol. This in turn, when evaporated, left a clear yellow oily substance.

Fig. 2.

At the time of the percolation described above, 50 Gm. of unripe and ripe drug were percolated separately with 50 per cent alcoholic menstruum. The volume was finally adjusted by evaporation, without heat, such that 1 cc. represented 1 Gm. of the drug.

A male cat weighing 2.8 Kg. was anesthetized with sodium amytal, administered intraperitoneally, and prepared in the manner of the previous experiments. After obtaining a control, 1 mg. per Kg. of atropine sulfate was administered intravenously. Allowing a sufficient length of time for the completion of this reaction, 1 cc. of the clear yellow oily substance from the petroleum-ether extraction, emulsified with saline, was administered intravenously. Since practically no effect was obtained from this dose, a larger dose, 2 cc., was administered. A definite depressor action was produced. Thereafter, repeated doses of 0.75 cc. of epinephrine hydrochloride (1:50,000), produced responses similar to those produced before the fraction was given. Since the petroleum-ether fraction neither inhibited nor augmented the activity of epinephrine hydrochloride, it appeared that this extractive must likewise contain the same depressor substance as was present in the 50 per cent alcoholic extraction. At this time 2 cc. of the 50 per cent alcoholic extraction of the unripe drug were injected. This produced a definite depressor effect. The effect of 0.75 cc. of the epinephrine hydrochloride solution was again apparently not modified. Repeated doses of both the extractive and epinephrine hydrochloride solution were given and these confirmed previous observations. A 2-cc. dose of the ripe drug extractive was then administered intravenously and the results obtained were almost identical with those obtained from the unripe drug. A repetition of the dose duplicated the original response. Two more 2-cc. doses of the unripe drug extractive were injected alternately with doses of 0.75 cc. of epinephrine hydrochloride solution. The results confirmed the previous observations on the activity of this preparation.

Using the same preparations of *Ustilago maydis* as were used in the above experiments upon cats, confirmatory evidence was obtained upon a dog. The animal was anesthetized with chloretone, administered intravenously. The animal also received 1 mg. per Kg. of atropine

sulfate. One cubic centimeter of ripe drug extractive was administered, which produced a slight pressor action. Following this a 2-cc. dose of unripe drug fluidextract produced the characteristic depressor effect.

The above observations indicated that the principle responsible for the depressor activity of *Ustilago maydis* is soluble in both 50 per cent alcohol and petroleum ether.

The presence of one or more alkaloids in *Ustilago* has been suggested from time to time by various workers. Since the above experiments indicated that the activity resided in a non-alkaloidal fraction (solubility in petroleum ether), this problem was pursued further.

One hundred grams each of ripe and unripe *Ustilago maydis* were thoroughly mixed and macerated with one liter of ethyl ether, which was added in 75-cc. portions over a period of two days. To this mixture, 30 Gm. of magnesium oxide were added to alkalinize the solution. After thoroughly shaking for approximately thirty minutes the solution was allowed to stand for separation of the layers. The ethereal solution was then drawn off and shaken with 1 per cent tartaric acid solution. The acidified aqueous portion was then separated and tested for the presence of alkaloids by the following alkaloidal methods: to a portion, on a spot plate, a drop of $N/10$ iodine test solution was added, yielding a very slight fine precipitate. Mayer's Reagent was then tried in the same manner and this produced an extremely fine precipitate which was barely perceptible. Finally, tannic acid was used as a test solution and a negative result was obtained.

The above acid-aqueous solution, which should have contained any alkaloids present in the drug, failed to produce any significant effect upon the isolated rabbit uterus in doses representing concentrations of the drug as high as 1:50 in the tissue chambers. Similarly this solution proved to be devoid of significant activity upon the carotid blood pressure of anesthetized cats.

The above tests, it is believed, rather conclusively show that the activity of the drug is not derived from constituents of an alkaloidal nature.

TABLE I.

Date.	Animal.	Weight.	Dose in Gm. of Drug.	Cc. of Fluid Injected.	Drug from Which Extraction Was Made and When Extracted.	Type of Solution.	Orig. Reading.	Reading 1 Hr.	Reading 2 Hr.	Reading 3 Hr.	Reading 4 Hr.	Reading 6 Hr.	Next Morn.	2nd Day.
11.16.34	White leghorn cockerel	1.95 Kg.	4.0 Gm.	0.8 cc.	Unripe 1934 Maryland, 7.25.34	25 per cent alcoholic	001	001	112	113	113	012	...	...
11.16.34	White leghorn cockerel	1.17 Kg.	3.75 Gm.	0.75 cc.	Unripe 1934 Maryland, 7.25.34	25 per cent alcoholic	001	001	112	112	112	011	...	...
11.16.34	White leghorn cockerel	0.80 Kg.	3.7 Gm.	0.74 cc.	Unripe 1934 Maryland, 7.25.34	25 per cent alcoholic	001	001	112	112	123	011	...	...
2.14.35	White leghorn cockerel	1.63 Kg.	4.0 Gm.	4.00 cc.	Unripe 1934 Maryland, 7.25.34	25 per cent alcoholic	012	012	012	012	...	...	...	...
10.27.36	White leghorn cockerel	1.87 Kg.	10.0 Gm.	1.00 cc.	Unripe 1936 Maryland	95 per cent alcohol	000	011	012	...	...	...	112	001
10.28.36	White leghorn cockerel	1.25 Kg.	20.0 Gm.	2.00 cc.	Unripe 1936 Maryland	95 per cent alcohol	000	100	111	...	...	...	001	001
10.29.36	White leghorn cockerel	1.87 Kg.	20.0 Gm.	2.00 cc.	Unripe 1936 Maryland	95 per cent alcohol	001	011	112	...	...	...	223	123
11.16.36	White leghorn cockerel	1.15 Kg.	5.0 Gm.	1.00 cc.	Ripe 1936 Maryland, 10.30.36	Oil fract. after evap. of alcohol	111	123	123	...	...	...	111	...

ACTION ON COCKSCOMB.

The cockerels used in the following experiments were those used routinely in this laboratory for assaying ergot by the U. S. P. method. Twenty-five cubic centimeters of a solution prepared by percolating a mixture of ripe and unripe drug with 50 per cent alcohol was evaporated to a semi-solid consistence, without heat, and then taken up in 1 cc. of 25 per cent alcohol. One cubic centimeter of this solution represented 5 Gm. of drug. Eight-tenths cubic centimeter of this solution was injected into the breast muscles of the cockerel. Into the second cockerel 0.75 cc. of a like solution was injected, representing 3.75 Gm. of drug. Into a third cockerel 0.74 cc. of a like solution was injected, representing 3.7 Gm. of drug. The results of these experiments may be seen in Table I. At a later date 4 cc. of fluidextract representing 4 Gm. of drug were injected into the breast muscles of a white Leghorn cockerel. The results of this experiment may be found in Table I. At the time of an evaporation of a 95 per cent alcohol percolate, some of this concentrate was injected into the breast muscles of a cockerel. One cubic centimeter of this solution, made from unripe drug was injected. The results may be seen in Table I. Two cubic centimeters of the same solution were injected into another bird. A comparison of the results showed a definite disagreement. One cubic centimeter of the solution represented 10 Gm. of drug. To check this work 2 cc. of the same solution were injected into the same bird which had received the 1-cc. dose and a positive response was noted. This showed that the threshold of the bird which first received the 2-cc. dose was much greater than the one receiving the 1-cc. dose. After evaporating the alcohol from the fluidextract the heavy viscid oily fraction remaining was used for the next test. One cubic centimeter of this substance, representing 5 Gm. of the drug, was injected into the cockerel which had originally received the 1 cc. of the fluidextract. The results may be seen in Table I.

From the above results it appears that some substance present in the drug caused a bluing of the combs of these cockerels. It was observed that this bluing was different from that of ergot in that there appeared to be a stasis of blood in the comb due to excessive dilatation rather than constriction of the blood vessels. Further, the blanching of the comb characteristic of ergot action was not observed, nor was there fluffing of the feathers (which is pronounced in ergot action). It appears, therefore, that although *Ustilago* can cause a cyanosis of the cockscomb, its action is relatively weak and possibly qualitatively dissimilar to ergot in this effect.

EFFECT OF USTILAGO ON PREGNANCY IN CATS.

A fluidextract was made from 500 Gm. of an equal mixture of ripe and unripe drug by percolation with 95 per cent alcohol until the drug was exhausted. The percolation of this preparation was preceded by forty-eight hours of maceration with the solvent. Following the percolation the solution was adjusted to fluidextract strength by evaporation with the aid of a current of air and without heat.

Table II embraces the results obtained in these experiments.

As may be seen in Table II, small doses of the drug failed to produce abortion and, furthermore, failed to produce any other symptoms of activity in the animals. By increasing the dosage sufficiently, an abortive action was clearly demonstrable. Of striking significance is the influence of the different solvents on the activity observed. The alcoholic extracts and the olive oil suspensions were possessed of definite abortive activity, whereas the aqueous solutions, prepared by removal of alcohol from the extracts without heat and diluting with water, and using only the clear supernatant aqueous liquid, were apparently quite devoid of any type of activity.

Although it was difficult to ascertain the stage of pregnancy in the animals, it was apparent that the drug was more effective in terminating early pregnancies than those approaching full term.

The depressor effects obtained in the earlier blood pressure experiments suggested the possibility of an acetylcholine or histamine-like principle as being responsible for the abortive action. However, the results in Table III show acetylcholine, even in enormous doses, to be ineffective in terminating pregnancy in the cat. The insolubility of the active principle in water also proves lack of similarity to cholines or histamine. That acetylcholine or histamine are quite devoid of significant oxytocic action has been shown in other reports from this laboratory (20).

TABLE II.

Date.	Cat Identity.	Dose in Gm. of Crude Drug.	Cc. of Fluid Injected and Area.	Drug from Which Ext. Was Made and Date of Extraction.	Type of Solution.	Result.	Remarks.
2.25.35	Black	0.5 Gm.	2 cc. Sub. Q. abdomen	R., U., equal parts, 2.15.35	Alcoholic	−	.....
2.25.35	Black	2.5 Gm.	5 cc. Sub. Q. abdomen	E. U.; L. U., L. R. in like parts, 2.15.35	Alcoholic	−	.....
7.8.35	Gray-white	30.0 Gm.	10 cc. Sub. Q. thigh	Equal parts R., U. percol. with fldext., 2.15.35	Alcoholic	+	3 hairless kittens dead
7.8.35	Black-white	30.0 Gm.	10 cc. Sub. Q. thigh	Equal parts R., U. percol. with fldext., 2.15.35	Alcoholic	+	2 kittens with hair at night 1 in morn., all dead
7.25.35	Maltese	10.0 Gm.	10 cc. Sub. Q. thigh	Equal parts R. and U., 3.25.35	Alcoholic	−	Close to term
7.25.35	Maltese	10.0 Gm.	10 cc. Sub. Q. thigh	Equal parts R. and U., 3.25.35	Alcoholic	+	3 kittens, fine hair, all dead
8.13.35	Grey	10.0 Gm.	10 cc. Sub. Q. thigh	Equal parts R. and U., 3.25.35	Alcoholic	−	Close to term
5.13.36	Black	100.0 Gm.	10 cc. Sub. Q. thigh	Equal parts, 1934–1935, collect., 4.23.36	Water emulsion	−	.....
5.14.36	Same as 5.13.36	100.0 Gm.	10 cc. Sub. Q. thigh	Equal parts, 1934–1935, collect., 4.23.36	Olive oil	+	4 kittens alive but from size cat not at full term
5.22.36	Maltese	100.0 Gm.	10 cc. Sub. Q. thigh	Equal parts, 1934–1935, collect., 4.23.36	Water emulsion	−	.....
5.25.36	Same as 5.22.36	100.0 Gm.	10 cc. Sub. Q. thigh	Equal parts, 1934–1935, collect., 4.23.36	Olive oil	−	Close to term
7.28.36	Maltese	20.0 Gm.	20.0 cc., 10.0 cc. Sub. Q. in each thigh	Equal parts, 1934–1935, collect , 5.27.36	Olive oil	+	Aborted during night, 7.29.36, 4 kittens about two weeks of pregnancy
11.18.36	Tiger stripe	33.0 Gm.	6.6 cc., Sub. Q. thigh	Ripe, 1936	Oil fraction after evap. of alcohol	−	Close to term. Animal died 11.21.36, without giving birth to kittens. Blood in nose and mouth

R. = Ripe; U. = Unripe; E. = Early; L. = Late; Collect. = Collection.

TABLE III.

Date.	Cat Identity.	Dose in Mg. of Drug.	Cc. of Fluid Injected and Area.	Type of Solution.	Result.
8.26.35	Grey	0.5 mg.	1 cc. Sub. Q. thigh	Aqueous	—
8.27.35	Same as 8.26.35	4.5 mg.	1 cc. Sub. Q. thigh	Aqueous	—
9.3.35	Same as 8.26.35	25.0 mg.	1 cc. Sub. Q. thigh	Aqueous	—
9.4.35	Same as 8.26.35	500.0 mg.	1 cc. Sub. Q. thigh	Aqueous	—

EFFECT OF USTILAGO ON CAT UTERUS IN SITU.

In attempting to record the drug action upon the non-pregnant uterus it was found that the tissue was non-responsive to varied doses of the drug when injected subcutaneously or intravenously. After six experiments upon six different cats this type of approach was abandoned

Experimental work upon the pregnant cat uterus *in situ* showed that there was a slight drug action, which, however, was not sufficiently consistent to accept as conclusive evidence of definite uterine activity. Inasmuch as a slight activity was noted it should be mentioned that the animals used were in the late stage of pregnancy. Animals in the earlier stages of pregnancy were not available for these experiments.

However, the experimental work upon the puerperal uterus *in situ* clearly showed oxytocic activity. The animal used in the experiment, illustrated in Fig. 3, had delivered two live kittens twenty-four hours before this experiment. The fluidextract used in this particular experiment

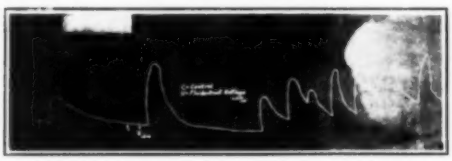

Fig. 3A.

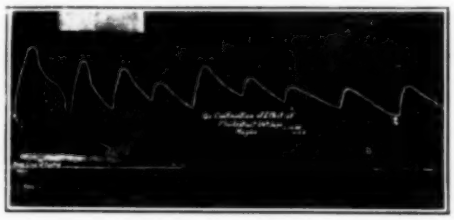

Fig. 3B.

was made from an equal mixture of ripe and unripe drug, percolated with 50 per cent alcohol. The animal was anesthetized with phanodorn (40 mg. per Kg.) which was administered subcutaneously. The drug was administered intravenously. As may be seen in Figs. 3A, B and C, the drug produced a definite action upon the uterus.

It not only increased the rhythmicity, but also the tonus of the muscle. It may further be seen that this preparation maintained this increased rhythm and tonicity over a considerable period. After recording this result a dose of fluidextract of ergot was given for comparative purposes. This drug further increased the rhythmicity and tonus of the muscle as shown in Fig. 3C.

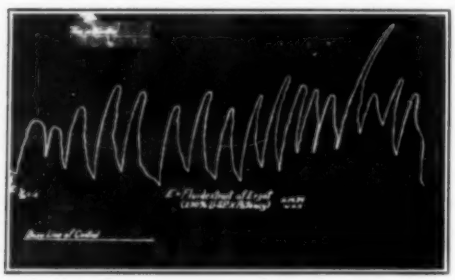

Fig. 3C.

EFFECT OF USTILAGO ON THE ISOLATED GUINEA-PIG UTERUS.

The tests upon isolated guinea-pig uteri involved the use of virgin guinea-pig uteri as in the U. S. P. assay for Solution of Posterior Pituitary. These strips of uteri were mounted in an isolated tissue bath, containing 50-cc. chambers for the 37.5° C. Locke-Ringer solution, in the conventional manner for this type of experiment.

The preparation to be tested consisted of mixed equal quantities of ripe and unripe drug collected in the fall of the year, approximately one month prior to the test. The drug was extracted with 95 per cent alcohol and then adjusted so that 1 cc. represented 1 Gm. of drug.

Before using this highly alcoholic solution, the alcohol was driven off and its volume replaced by distilled water, the dilution forming an emulsion. A U. S. P. Solution of Posterior Pituitary was

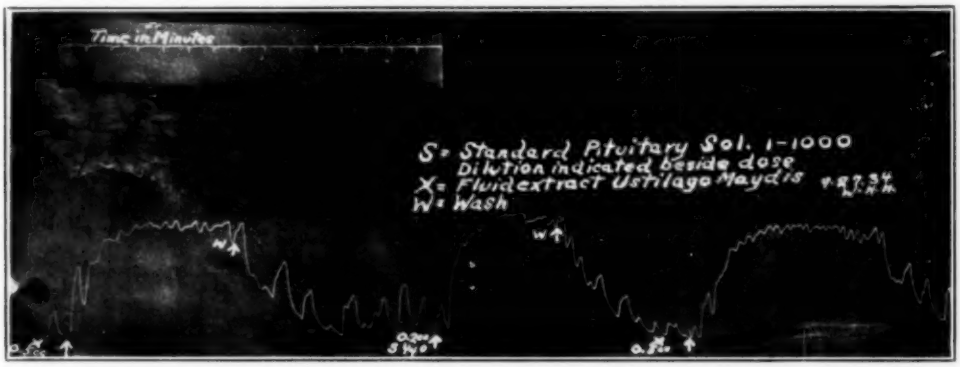

Fig. 4.

used as a means of comparison. Figure 4 clearly shows the results of the action of this preparation upon the guinea-pig uterus.

It may be seen that this fluidextract, although much weaker than the pituitary solution, definitely possessed a stimulating influence upon the isolated guinea-pig uterus, qualitatively comparable to that of pituitary. Based on this experiment, 1 cc. of U. S. P. Solution of Posterior Pituitary was equivalent in activity to approximately 80 Gm. of Ustilago.

EFFECT OF USTILAGO ON THE ISOLATED RABBIT UTERUS.

The preparation of drug used was the same as that used in the preceding experiment, except that 1 cc. represented 200 mg. of drug. A solution of epinephrine hydrochloride (1–10,000) was used as a comparative drug for these experiments.

The activity of the drug upon this type of tissue may be seen in Fig. 5.

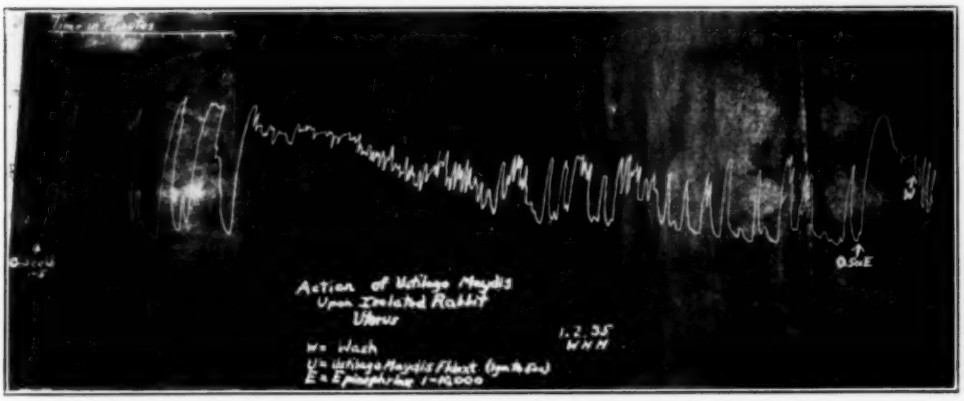

Fig. 5.

Since the action of epinephrine hydrochloride solution was not diminished, it is apparent that the principle which is responsible for the oxytocic activity of Ustilago does not resemble ergotamine or ergotoxine, both of which inhibit the epinephrine activity.

THE EFFECT OF USTILAGO ON ISOLATED RABBIT INTESTINE.

The fluidextract of *Ustilago maydis* employed in all of the experiments upon isolated rabbit intestine was prepared from equal mixtures of one- and two-year old ripe and unripe drug. The menstruum used was 95 per cent alcohol. After percolation to exhaustion of the drug the alcohol

was driven off by a current of air, without heat and the volume restored with distilled water to make the preparation of fluidextract strength. Upon adding water to this extract a milky emulsion formed, which, upon standing, broke down yielding a pale yellowish to light orange-colored aqueous layer and a gummy resinous layer. This same condition was noted in the uterine experiments. Consequently, the solution was constantly agitated to maintain the emulsion form which was utilized in the experiments. These layers were also studied separately in order to determine which of the layers carried the active substance.

Histamine and acetylcholine were administered to determine whether or not the results obtained in the previous isolated tissue experiments were caused by a similar or different principle.

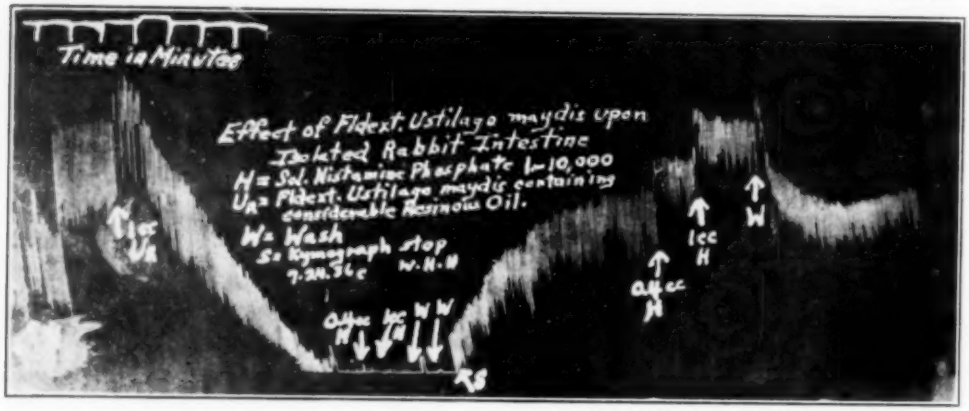

Fig. 6A.

Time in Minutes
W
4cc
S
Effect of Fldext. Ustilago maydis upon
Isolated Rabbit Intestine
C= Control H= Sol. Histamine Phosphate 1-10,000 W= Wash
Ux= Fldext. Ustilago maydis containing a slight amount of Resinous Oil
S= Kymograph Stop

Fig. 6B.

Having obtained the action of both histamine and acetylcholine, a portion of the aqueous layer, containing a slight amount of the oily substance, was administered. The drug first stimulated and then gradually inhibited the intestinal movements.

Since this aqueous layer possessed little or no convincing action upon the isolated rabbit intestine it was decided to administer some of the resinous oily portion in the form of an aqueous emulsion. The same technique was used except that the administration of acetylcholine was omitted.

It was observed that this resinous oily substance contained a principle which abolished the activity of the intestine and also the stimulant effect of histamine phosphate solution. Further,

a dose exceeding twice the original stimulating dose of histamine failed to initiate a response. After washing the tissue with Tyrode's (the solution utilized in all of the intestinal experiments) the rhythmicity and tonus of the tissue returned. Another experiment was performed to check the above result, using one-half the quantity of the emulsion. The expected response was obtained. Finally, to check these two results a fresh piece of tissue was mounted in the bath and, after the administration of the histamine, first the aqueous portion containing a slight amount of the resinous oil was administered, then after the tissue returned to the control level the resinous oil was administered in the emulsion form. Figures 6A and B illustrate the results. From these experiments it may be concluded that the activity of this preparation was contained for the most part in the resinous oily portion.

EFFECT OF USTILAGO ON THE PERFUSED LEG VESSELS OF THE FROG.

The method employed for the perfusion experiments was that of Lewen-Trendelenberg (21). The preparation employed in this work was the same alcohol-free fluidextract as was employed in the intestinal experiments. One cubic centimeter of the solution representing a dilution of 1–100 of the fluidextract was perfused through the vessels. The rate of flow remained practically unchanged. After injecting the second 1-cc. dose a definite slowing of the flow was observed, which after a few minutes increased slightly above the control rate.

It was observed that this increased rate was maintained for approximately ten minutes, at which time 1 cc. of the undiluted fluidextract was administered. This immediately slowed the rate of flow from approximately nine down to five drops per minute. Thus it may be concluded that the fluidextract, by this particular perfusion method, has a weak action in constricting the leg vessels of the frog.

TOXICITY OF USTILAGO.

Since the cat was used as the test animal for uterine and abortion studies, this animal was the logical choice for the investigation of the toxicity of *Ustilago maydis*. Table IV embraces a concise yet comprehensive résumé of the toxicity experiments. It may be noted that three of the recorded deaths involved pregnant animals. These animals are included here as well as in Table II, inasmuch as they died while under the influence of *Ustilago maydis* in an attempt to induce abortion.

The toxicity of *Ustilago maydis*, by oral administration, was also investigated by feeding mature white rats a mixture of fifty per cent stock rat food and fifty per cent *Ustilago maydis*.

The animals were at first limited to a definite quantity per day, but since there was a general daily decline in weight this plan was abandoned in favor of a surplus feeding. Immediately upon the increased feeding the animals showed a daily increase in weight over a period of three months and apparently maintained their normal health.

Therefore, it appears from the above experiment that *Ustilago maydis* is very low in toxicity when fed to non-pregnant rats. The influence of feeding the drug to pregnant animals is being studied further.

SUMMARY.

Ustilago maydis, ripe and unripe, has been studied by a variety of pharmacological procedures for the purpose of determining the presence or absence of activity in this drug, and the qualitative nature of this activity.

CONCLUSIONS.

1. *Ustilago maydis*, when administered intravenously in an aqueous suspension of a hydro-alcoholic fluidextract, produces a depressor effect upon the carotid blood pressure of the cat and dog without significantly inhibiting the pressor activity of epinephrine.

2. Ripe and reasonably mature unripe samples of *Ustilago maydis* appeared to be of equal activity.

3. It was impossible to demonstrate, by the methods employed, the presence of any active alkaloid in *Ustilago maydis*.

TABLE IV.

Date.	Type of Animal and Wt.	Dose in Gm. of Drug.	Cc. of Fluid Injected and Area.	Drug from Which Ext. Was Made. Date of Ext.	Type of Solution.	Result.	Remarks.
4.20.36	Maltese pregnant, 2.55 Kg.	500 Gm.	20 cc. Sub. Q. thigh	1935 Md., 1934 Md., 1935 Io., E. P.	A. 10 cc., 0. 10 cc.	+	10 cc. A., R. T., 10 cc. O., L. T.
5.7.36	Maltese female, 2.35 Kg.	400 Gm.	30 cc. Sub. Q. thigh	1934 Md., 1935 Md., E. P.	A. 10 cc., O. 10 cc.	+	10 cc. of three percola.
7.30.36	Maltese pregnant, 2.40 Kg.	400 Gm.	10 cc. Sub. Q. thigh	1934 Md., 1935 Md., E. P.	Olive oil	+	.....
7.30.36	Stripe female, 1.95 Kg.	400 Gm.	10 cc. Sub. Q. thigh	1934 Md., 1935 Md., E. P.	Olive oil	+	.....
11.18.36	Stripe pregnant, 3.00 Kg.	33 Gm.	6.6 cc. Sub. Q. thigh	1936 Md., ripe	Oil frac. after evap.	+	Animal died 11.21.36
12.2.36	B. and W. female, 1.50 Kg.	100 Gm. per Kg.	4.5 cc. I. M. thigh	1936 Md., ripe	P. E. ext. taken up in O	−	.....
12.2.36	T. and W. female, 1.77 Kg.	50 Gm. per Kg.	2.66 cc. I. M. thigh	1936 Md., ripe	P. E. ext. taken up in O	−	.....
12.7.36	B. and W. female, 1.50 Kg.	100 Gm. per Kg.	9.6 cc. I. P.	1936 Md., ripe	Al. ext. in O	+	.....
12.7.36	T. and W. female, 1.67 Kg.	120 Gm. per Kg.	13 cc. I. P.	1936 Md., ripe	Al. ext. in O	+	.....
12.8.36	B. and W. female, 1.05 Kg.	50 Gm. per Kg.	3.2 cc. I. P.	1936 Md., ripe	Al. ext. in O	−	.....

TABLE IV.—(*Continued from page 750*).

Date.	Type of Animal and Wt.	Dose in Gm. of Drug.	Cc. of Fluid Injected and Area.	Drug from Which Ext. Was Made. Date of Ext.	Type of Solution.	Result.	Remarks.
12.8.36	Maltese male, 1.55 Kg.	100 Gm. per Kg.	6.5 cc. I. P.	R. and U., Md., 1936	Al. ext. in O	+	.....
12.8.36	B. and W. female, 1.45 Kg.	200 Gm. per Kg.	12 cc. I. P.	R. and U., Md., 1936	Al. ext. in O	+	.....
12.21.36	Stripe female, 1.40 Kg.	50 Gm. per Kg.	4.2 cc. I. P.	Ripe, 1936	Al. ext. in O	−	.....
12.21.36	B. and W. female, 1.76 Kg.	75 Gm. per Kg.	8 cc. I. P.	Ripe, 1936	Al. ext. in O	+	.....
12.21.36	G. and W. female, 1.63 Kg.	100 Gm. per Kg.	10 cc. I. P.	Ripe, 1936	Al. ext. in O	+	.....
12.22.36	Black female, 2.20 Kg.	100 Gm. per Kg.	14.5 cc. I. P.	Unripe, 1936	Al. ext. in O	−	.....
12.22.36	B. and W. female, 1.70 Kg.	50 Gm. per Kg.	5.6 cc. I. P.	Unripe, 1936	Al. ext. in O	−	.....
1.5.37	Black female, 1.85 Kg.	200 Gm. per Kg.	14.8 cc. I. P.	Unripe, 1936	Al. ext. in O	+	.....
1.5.37	Grey female, 1.95 Kg.	150 Gm. per Kg.	11.7 cc. I. P.	Unripe 1936	Al. ext. in O	+	.....

Sub. Q. = Subcutaneous; I. M. = Intramuscular; I. P. = Intraperitoneal; B. = Black; W. = White; T. = Tan; G. = Grey; A. = Aqueous; Al. = Alcohol; E. P. = Equal Parts; Io. = Iowa; O = Olive Oil; R. = Ripe; U. = Unripe; R. T. = Right Thigh; L. T. = Left Thigh; ext. = extraction.

4. Tested by the U. S. P. Cockscomb method for Ergot, Ustilago produces a cyanotic reaction, but relatively large doses were required. The cyanosis, as well as the symptoms induced in the cockerels, differed considerably from the effects produced by Ergot.

5. Ustilago causes abortion in cats especially in the early stages of pregnancy. Quantitatively this drug is many times weaker than Ergot in this respect.

6. The active substance of *Ustilago maydis* is not of an acetylcholine or histamine-like nature.

7. It can be demonstrated that *Ustilago maydis* causes contractions of the pregnant and puerperal cat uterus *in situ*.

8. *Ustilago maydis* stimulates contractions of the isolated guinea pig and the rabbit uterus.

9. *Ustilago maydis* inhibits the movements of isolated rabbit intestine as well as the stimulating effect induced by solutions of histamine phosphate.

10. It has been found after fractional separation of the alcoholic fluidextract of *Ustilago maydis*, that the greater portion of the activity resides in the resinous oily-like fraction rather than in the aqueous fraction. Petroleum-ether extracts have been found to possess the same activity as that of alcoholic extracts.

11. *Ustilago maydis* preparations have been found by perfusion experiments to produce a constriction of the leg vessels of frogs.

12. *Ustilago maydis* exhibits toxicity when administered intramuscularly, intraperitoneally or subcutaneously to cats. By the subcutaneous or intramuscular route, doses equivalent to 400 Gm. of drug were required to kill, whereas intraperitoneal injections produced death in doses equivalent to approximately 75 Gm. of drug.

13. *Ustilago maydis* when fed to mature non-pregnant white female rats failed to show any significant toxicity.

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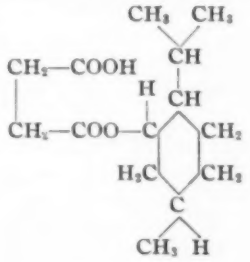
STUDIES ON THE PREPARATION AND TOXICITY OF MENTHYLSUCCINIC ACID AND ITS HEAVY METAL SALTS.*

BY W. M. LAUTER AND V. L. VRLA.

Mono-menthyl-succinic acid was first described by Zelikow (1) and Arth (2) and its silver salt prepared. It had been noted previously (3) that mono-esters of poly-carbonic acids frequently form heavy metal salts which have the faculty of being soluble in vegetable oils, such as olive, sesame, peanut and sweet almond. It was also noted that this oil solubility seemed to increase with the increase in the chain length of the alcohol which forms such a mono-ester. It was to be expected therefore that heavy metal salts of mono-menthylsuccinic acid might be soluble in vegetable oils.

PREPARATION OF MENTHYLSUCCINIC ACID.

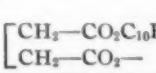


900 Gm. succinic acid and 720 Gm. menthol were heated for three hours in an oil-bath at 175–180° C. After cooling, 1500 cc. 95% alcohol were added. This was filtered and washed with a little alcohol. 267.8 Gm. succinic acid were recovered. The alcoholic solution was poured into a solution of 434 Gm. $Na_2CO_3.H_2O$ in 15 liters of water. The insoluble material was filtered and washed with water. 205.5 Gm. remained which, after recrystallization from methanol, gave a melting point of 63.5° C. The melting point of di-menthyl-succinate is 64° C. Therefore, this substance, insoluble in Na_2CO_3 is di-menthyl-succinate.

The clear filtrate was slowly acidified with 393 Gm. H_2SO_4, dissolved in 2 liters of water. After cooling the precipitate was filtered off, washed with water and dried. The yield was 845.7 Gm., and the melting point was 54–56° C. Further purification was done by redissolving in a solution of 219.2 Gm. $Na_2CO_3.H_2O$ in 4000 cc. water and shaking out with ether. The water solution was then reprecipitated with dilute sulfuric acid. Yield: 699.3 Gm., melting point 62° C. The yields were as follows:

Succinic acid recovered	29.80%
Succinic acid in yield of menthyl-succinate	35.80%
Succinic acid in yield of di-menthyl-succinate	6.84%
Succinic acid accounted for	72.44%
Menthol in yield of menthyl-succinate	59.20%
Menthol in yield of di-menthyl-succinate	22.54%
Menthol accounted for	81.74%

Bismuth-tri-menthyl-succinate.



* From the Research Department of R. J. Strasenburgh Co., Rochester, N. Y.

769 Gm. menthylsuccinic acid (3 mols) were dissolved in 300 cc. warm ethanol and poured into a solution of 186 Gm. $Na_2CO_3.H_2O$ ($1^1/_2$ mols) in 400 cc. H_2O. To this solution was added, while stirring, at a temperature of 60° C., a solution of 481.5 Gm. Bi $(NO_3).5H_2O$ (1 mol) dissolved in 3000 cc. H_2O and 2400 cc. glycerine. The semi-solid precipitate was washed by decantation with water. The precipitate was taken up with 2000 cc. ether and the ether solution was washed several times with water and then dried with Na_2SO_4. After evaporation of the ether, a yield of 974.6 Gm. (85.5% yield) was obtained. The heavy yellow viscous material was assayed.

21.35% Bi found
21.45% Bi calculated.

This material was soluble in ethanol, menthanol, acetone, olive oil and oil of sweet almonds. It was insoluble in water.

TOXICITY TESTS FOR BISMUTH-TRI-MENTHYL-SUCCINATE (INTRAMUSCULARLY).

No. of Rats.	Mg. Metallic Bismuth per Kg. Body Weight.	Results.
6	250	4 died within 12–20 days 2 recovered
6	220	4 died within 13 days 2 recovered
6	175	All 6 remained alive

This shows that the toxicity was approximately 200 mg. Bi per Kg. body weight.

Basic Bismuth-Menthyl-Succinate.—When a sample of bismuth-tri-menthyl-succinate was treated with 85% methanol, a white solid material was formed which proved to be insoluble in absolute methanol. Its melting and decomposition point was 206° C. When dissolved in chloroform and poured into methanol, it could be reprecipitated. When over-heated, menthol odor could be detected. The analysis was 43.18% Bi.

Calculated for $\begin{matrix} CH_2—CO_2—C_{10}H_9 \\ | \\ CH_2—CO_2—Bi(OH)_2 \end{matrix}$ = 43.53% Bi

Manganese-Di-Menthyl-Succinate.—51.25 Gm. menthyl succinate (1/5 mol) dissolved in 500 cc. distilled water, containing 12.4 Gm. $Na_2CO_3.H_2O$ ($^1/_{10}$ mol). 44.5 Gm. manganese gluconate ($^1/_{10}$ mol) dissolved in 300 cc. water were added to the sodium-menthyl-succinate solution. A fine precipitate was formed which was taken up with ether. After washing, the ether solution was subjected to distillation. The residue (40.2 Gm.) was a pink powder and melted at 168–170° C.

Assay:

9.72% Mn found
9.71% Mn calculated for

$$\left(\begin{matrix} CH_2.CO_2.C_{10}H_9 \\ | \\ CH_2.CO_2— \end{matrix}\right)_2 Mn$$

The salt was insoluble in water, soluble in ether, chloroform and ethanol. Its solubility in cold olive oil and cotton seed oil was very low. However, 100 cc. of an olive oil solution containing 5% camphor dissolved 5.6 Gm. manganese-di-menthyl-succinate.

Silver-Menthyl-Succinate.—As stated previously, this product had been mentioned but not described in the literature. It was prepared as usual by reacting silver nitrate ($^1/_5$ mol) with sodium-menthyl-succinate ($^1/_5$ mol). A fine white powder was obtained. After drying for 1 hour at 100° C., the following silver assay was obtained.

29.65% Ag found
29.70% Ag calculated for

$AgCO_2—CH_2—CH_2—CO_2C_{10}H_{19}$

The melting point was 104° C. This salt appeared to be insoluble in vegetable oils and very little soluble in ethylene glycol and di-ethylene-glycol.

Attempts to prepare stable neutral lead and mercury salts of menthylsuccinic acid did not prove to be successful, if the above-mentioned method of preparation was employed. The lead salts obtained were basic salts and no definite salt could be isolated. The mercury compound obtained was found to be a menthylsuccinic acid mercuric chloride. When prepared from $^1/_8$ mol of sodium menthyl-succinate solution and $^1/_{10}$ mol HgCl in aqueous solution, a yield of 41.1 Gm. of a white salt was obtained. After two recrystallizations from methanol a product with the following assay was obtained.

Found:

40.37% Hg
7.14% Cl

Calculated:

40.83%
7.22% for

$$\begin{array}{l} CH_2.CO_2C_{10}H_{19} \\ | \\ CH_2.CO_2.HgCl \end{array}$$

This salt was easily soluble in methanol, acetone and iso-propanol.

SUMMARY.

1. The bismuth, manganese, silver and mercury salts of menthylsuccinic acid were prepared and investigated for their faculty to dissolve in vegetable oils.

2. The bismuth and manganese salts were soluble, while the silver and mercury salts obtained were not.

3. The toxicity of the bismuth compound was approximately 200 mg. of metallic bismuth per Kg. body weight, when injected intramuscularly.

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THE SOLUBILITY OF LYOPHILE GELATINS.*

BY L. F. TICE.[1]

The ordinary commercial gelatins commonly employed are not, generally speaking, soluble to any appreciable extent in water at 25° C. When placed in water such gelatins absorb water to a considerable degree and become greatly swollen, but the individual particles originally present do not lose their identity nor have their number reduced. What has been interpreted as partial solubility by some workers is probably best explained as the exosmosis of lower molecular weight hydrolysis products from the swollen gelatin particle and their subsequent presence in the external aqueous medium. This seems borne out by the fact that gelatins of very low Bloom test, which are considerably hydrolyzed during manufacture, are actually found to slowly but completely dissolve in water at 25° C.

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[1] Department of Pharmacy, Philadelphia College of Pharmacy and Science.

During the past year the writer has had the opportunity to study several samples of gelatin prepared in dry solid form by the so-called "Lyophile" process. It is the purpose of this paper to report the unusual features of this material and to discuss the effect of a number of variables on its solubility in water.

The "Lyophile" process has been developed by the efforts of several workers. Reichel, Masucci and Boyer (1) perfected a method for its application to serums and biologicals in bulk. Flosdorf and Mudd (2) modified the apparatus used in the production of bulk material in such a manner as to make it applicable to individual ampul packages. This apparatus has since been improved and perfected by Dr. John Reichel and his co-workers at the research laboratories of Sharp & Dohme. The process in brief consists of the rapid freezing of an aqueous solution followed by dehydration of the frozen material under high vacuum. The solution is frozen at −78° C. in a shell in very large Pyrex or metal bulbs which are connected to a large bulb condenser at a distance from the containers. This condenser is surrounded by a refrigerant bath of solid CO_2 in acetone or methyl cellosolve. The material is kept in the frozen state solely by the rapid sublimation *in vacuo* of water vapor from its surface. The outer surfaces of the containers are surrounded merely by the air of the room at ordinary temperature during all of the dehydration process.

In preparing a series of lyophile gelatins, three samples of commercial gelatin were selected as follows:

	Precursor.	Jelly Strength.	pH.
#1	Bone	250 Bloom	6.0
#2	Porkskin	250 Bloom	4.4
#3	Porkskin	50 Bloom	4.4

Gelatins #1 and #2 represent high test gelatins from the two different precursors whereas #3 was a low test gelatin from the same precursor as #2. A corresponding low test gelatin from bone was not employed due to the unsatisfactory color and clarity observed in such material. Using these representative gelatins, warm solutions of varying concentrations were prepared and these were then frozen and dried by the lyophile process. In each case solutions whose concentrations were beyond a certain point could not be processed due to gelation of the material before it could be frozen. As would be expected, the low test gelatin could be prepared in higher concentration than the high test samples without gelation resulting during freezing.

The physical properties of lyophile gelatin are quite unusual. It is a pure white, extremely porous solid, easily compressed, very hygroscopic but not deliquescent, and exhibiting solubility features entirely different from ordinary gelatin. When examined microscopically, it appears to possess a mesh-like structure, the size of the openings decreasing with increased concentration of the solution processed. It is not believed that this observed structure is peculiar to gelatin since other materials yield porous bodies in lyophile form which are not subject to gelation. Lyophile gelatin is very bulky and porous making its apparent density extremely small. This is particularly true in cases where very dilute solutions were dried, the more concentrated solutions giving a denser product.

By far the most interesting feature of several of these gelatins was their complete and rapid solubility in water at 25–28° C. When one considers that in each case, regardless of the solution processed, the resultant product was pure dry gelatin this solubility is indeed unusual. If all of the lyophile gelatins had been uniformly soluble or if only those prepared from a low test gelatin were soluble the explanation would have been relatively simple, since it would be easily explained on the basis of increased surface area only. This not being the case an attempt was made to correlate the many variables in so far as their effect on the solubility was concerned.

In all of the series of gelatins prepared some of the gelatin was soluble in water; the difference noted was that in some cases it was completely soluble in a rela-

tively short time whereas in others hydrated masses were formed which persisted for a long period without going into solution.

The following experimental samples were prepared in bulk for examination:

A	0.2% gelatin #1	H	1.0% gelatin #2
B	0.5% gelatin #1	I	2.0% gelatin #2
C	1.0% gelatin #1	J	0.1% gelatin #3
D	2.0% gelatin #1	K	0.2% gelatin #3
E	0.1% gelatin #2	L	0.5% gelatin #3
F	0.2% gelatin #2	M	1.0% gelatin #3
G	0.5% gelatin #2	N	2.0% gelatin #3
		O	5.0% gelatin #3

In addition, several identical samples were processed in individual "vacuoles" since, in this type of evacuated ampul, solution of the material may be accomplished without preliminary exposure to air or moisture. This was done to determine the effect, if any, of these variables on the product.

The results are summarized as follows:

In Samples J to O, inclusive, wherein the low Bloom porkskin was used, all were easily soluble in water at 25° C. This would be expected due to the inherent solubility of the initial gelatin in water at the same temperature. The effect here is plainly one of increased surface, resulting in easy and rapid solution.

With the samples prepared with #1 and #2 gelatin, however, considerable differences were noted compared with both #3 and each other. Samples E and F corresponding to 0.1% and 0.2% of #2 were easily soluble in water at 25° C. while the higher concentrations required standing over night at 25° C. in order to completely dissolve. At 28° C. Samples G and H, representing 0.5% and 1.0% of #2, were easily soluble; and at 30° C. Sample I dissolved without difficulty. With samples prepared with gelatin #1 very poor solubility was found. For example, A prepared from 0.2% of #1 required a temperature of 28° and considerable time for solution to be complete. B, C and D were not completely soluble except when the temperature approached 35° C.

The solubility of samples made with gelatin #2 which was not observed in the case of the initial commercial material even on long standing, is probably explainable on the basis of increased surface area coupled with the theory that the rapid freezing prior to dehydration did not permit extensive aggregation of the gelatin molecules to the extent that an insoluble aggregate was reached. Since gelation is largely a process of molecular aggregation to form a network structure and one requiring an appreciable time for completion, then such aggregation would be materially prevented if cooling was rapid and the concentration of gelatin in solution was relatively low.

The greater difficulty experienced in dissolving those samples prepared from more concentrated solutions and, consequently, containing many more gelatin molecules is probably best explained by assuming that a greater degree of aggregation had taken place prior to complete freezing.

The difference in behavior of samples from gelatin #1, as compared with those from gelatin #2, may be explained by the fact that the p_H of #1 gelatin (6.0) lies so near to its isoelectric point, approximately 4.7, that it possessed less affinity for water and was, consequently, less soluble than corresponding samples made from #2 whose p_H (4.4) is considerably removed from its isoelectric zone of about 7.5.

In addition to the foregoing results the following observations were also made concerning the behavior of lyophile gelatin:

1. The ease of solution is increased when the ratio of solvent to gelatin is small. Since lyophile gelatin is practically anhydrous and possesses a marked affinity for moisture, when only a small amount of water is employed a measurable elevation in temperature results, thus facilitating solution.

2. The use of rapid agitation during the addition of water greatly aids solution. This is a factor favoring the individual evacuated ampuls as when water is injected into them extremely vigorous agitation results.

3. Compression of the porous material does not alter its solubility but retards the rate somewhat due to a decrease in surface area exposed to the solvent.

4. Exposure to air was found to reduce the ease with which a given sample could be dissolved.

5. The lyophile process does not apparently alter the jelly strength of the gelatin so treated. When 5 per cent gels of the initial gelatins were prepared and compared with 5 per cent gels made with the lyophile product no difference in jelly strength could be detected.

6. Although samples prepared in "vacuoles" were, in general, easier to dissolve than identical bulk samples, in some few cases small films of insoluble material were observed which would not dissolve even upon heating. The significance of these is being investigated.

With ordinary gelatins, after a solution is made some considerable reduction in temperature is required in order for gelation to take place. However, by the use of a soluble lyophile gelatin a phenomenon of considerable interest to the colloid chemist may be accomplished, namely, what is in effect an isothermic sol→gel transformation. Five grams of a lyophile gelatin (sample F) are slowly dissolved in water at 25° C. in such a manner as to avoid any appreciable rise in temperature. The resulting solution when allowed to stand at the same temperature will slowly set to form a firm jelly. One might go even a step further and prepare a sol at a given temperature, then raise the temperature a few degrees and have a gel form. Obviously, the temperature at which the solution is allowed to stand must not approach too closely 35° C., the temperature at which gelatin can exist only in the sol state.

CONCLUSIONS.

1. The properties of lyophile gelatin have been investigated and in particular its solubility behavior.

2. Some explanations are advanced for the effect of several variables on the solubility of lyophile gelatin.

3. The change of gelatin from the dry solid state→sol→gel with the temperature being maintained constant is described.

ACKNOWLEDGMENT.

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DEGRADATION STUDIES ON DIBENZOYL DISULFIDE.*

BY E. S. COOK[1] AND KARL BAMBACH.[1]

The use of dibenzoyl disulfide as an antipuritic (1) has led to the recent study of satisfactory methods of synthesis (2), (3). We were further interested in studying the degradation of dibenzoyl disulfide by various methods in order to obtain quantitative conversion to a simple derivative which might supplement the routine Parr bomb sulfur analysis. Several procedures were tried before a successful quantitative degradation to benzoic acid was accomplished. This degradation was mentioned briefly in the paper of Shelton and Rider (2) but it seems worth while to pre-

* Presented before the Scientific Section, A. PH. A., New York meeting, 1937.

[1] From the Research Laboratories of The Wm. S. Merrell Company, Cincinnati, Ohio.

sent it in more detail. At the same time the other degradation studies will be summarized briefly since they are revealing as to the stability of dibenzoyl disulfide and the reactions in which it will take part.

(*1*) *Conversion to Benzanilide.*—Dibenzoyl disulfide is readily converted to benzanilide by refluxing in benzene (4) or in alcohol (benzanilide is soluble in hot alcohol but very slightly soluble in benzene):

$$C_6H_5COSSCOC_6H_5 + 2C_6H_5NH_2 \rightarrow 2C_6H_5CONHC_6H_5 + H_2S + S$$

This reaction, although apparently quantitative, did not lend itself to practical use because it was impossible completely to free the benzanilide from sulfur. Hence, attempts were made to hydrolyze the benzanilide to benzoic acid. This could not be accomplished quantitatively by aqueous or alcoholic alkali or by 50% (*w/v*) sulfuric acid. Five hours' refluxing with 75% (*w/v*) sulfuric acid brought about the hydrolysis but it was impossible to obtain consistent results. This resistance to hydrolysis is in accord with the recently published observation of Asinger (5) that benzanilide is only 50% hydrolyzed on 16 hours' boiling with methyl alcoholic potassium hydroxide.

The preparation of the more easily hydrolyzed benzamide by reaction of dibenzoyl disulfide with ammonia is complicated by the formation of ammonium thiobenzoate (4*b*) together, in our experience, with other by-products, and was not further investigated:

$$C_6H_5COSSCOC_6H_5 + 2NH_3 \rightarrow C_6H_5CONH_2 + C_6H_5COSNH_4 + S$$

(*2*) *Oxidation with Potassium Permanganate.*—It was thought that the use of a reagent which would convert all of the sulfur into a non-interfering form, such as sulfate, might be of value. Alkaline permanganate is recommended as a reagent which will oxidize sulfur completely to sulfate in organic sulfur compounds where sulfur is not attached to oxygen (6), (7). However, an excessive amount of permanganate ($9^1/_2$ moles) was necessary to react all of the dibenzoyl disulfide and this undoubtedly led to too extensive degradation and only about 35% of the theoretical amount of benzoic acid was obtained. Of course, sulfur could be determined after this treatment by the usual barium sulfate procedure but the simpler Parr bomb method is to be preferred.

(*3*) *Direct Hydrolysis to Benzoic Acid.*—Dibenzoyl disulfide may be hydrolyzed to a mixture of benzoic and thiobenzoic acids (2*a*):

$$C_6H_5COSSCOC_6H_5 + 2KOH \rightarrow C_6H_5COOK + C_6H_5COSK + S + H_2O$$

The thiobenzoic acid can then be converted to benzoic acid by further hydrolytic treatment giving a total of two molecules from one molecule of dibenzoyl disulfide. Saturated alcoholic potassium hydroxide did not complete the conversion to benzoic acid after boiling for 30 hours. Sodium ethylate, as might be expected, was likewise ineffective and gave a mixture of by-products. Dibenzoyl disulfide is remarkably resistant to acid hydrolysis, complete breakdown not occurring after 24 hours' boiling with 75% (*w/v*) sulfuric acid; benzaldehyde was detected among the products of reaction. Five and 25 per cent aqueous potassium hydroxide do not give quantitative yields of benzoic acid after 30 and 6 hours' boiling, respectively. Forty per cent aqueous potassium hydroxide, however, is entirely satisfactory in 3 hours and was the reagent chosen. Typical results are shown in Table I. The use of stronger alkali is disadvantageous since the solubility of potassium benzoate is so decreased that the reaction mixture does not remain fluid.

TABLE I.—BENZOIC ACID FROM DIBENZOYL DISULFIDE BY HYDROLYSIS WITH 40% AQUEOUS POTASSIUM HYDROXIDE.

Wt. Disulfide Gm.	Wt. Benzoic Acid Obtained Gm. (Theory = 0.890 Gm.)	Per Cent of Theory Obtained.
1	0.871	98.0
1	0.883	99.2
1	0.875	98.3

PROCEDURE FOR CONVERSION OF DIBENZOYL DISULFIDE TO BENZOIC ACID.

Reflux 1 Gm. of dibenzoyl disulfide and 30 cc. of 40% *w/v* potassium hydroxide solution in a 100-cc. round bottom flask for three hours. Cool, transfer to a Squibb separatory funnel (rinsing out flask with water), acidify with concentrated hydrochloric acid, and allow to cool again. Shake the benzoic acid into ether, using five portions (total of 120 cc.) and collect the ether extracts in another separatory funnel. Wash the ether with 25 cc. of approximately 0.1*N* hydrochloric acid, and then wash this aqueous portion with 15 cc. of ether. Combine the ether extracts and filter through cotton into a beaker, washing the cotton with fresh ether. Evaporate the ether with the aid of a stream of air. (Evaporation may be hastened by placing the beaker in a water-bath at not over 40° C. until 30 cc. remains; then remove from water-bath and complete removal with air.) Treat the residue with a solution of 1.5 Gm. of sodium bicarbonate in 50 cc. of water. Warm the mixture and allow it to stand until all the benzoic acid has dissolved; the sulfur will be practically insoluble. Filter the liquid through a coarse filter paper into a Squibb separatory funnel and wash the paper thoroughly with water. Acidify the sodium benzoate solution with 10% hydrochloric acid, allow it to cool, and shake out the benzoic acid with chloroform, using five portions (total of 100 cc.). Collect the chloroform extracts in another separatory funnel. Wash the chloroform with 20 cc. of approximately 0.1*N* hydrochloric acid, and then wash this aqueous portion with 10 cc. of chloroform. Filter the combined chloroform extracts through cotton into a tared beaker and evaporate the chloroform with the aid of a stream of air, placing the beaker in a water-bath at a temperature of not over 40° C. as before. Dry the benzoic acid over night in a vacuum over sulfuric acid and weigh.

In the above procedure ether is used for the first extraction since sulfur is much less soluble in it than in chloroform. The benzoic acid can be identified by melting point and the usual tests. The method in our hands has given consistent results of from 98% to 99.2% of the theoretical yield of benzoic acid which is within the limits of error of the shake-out.

One other method of degradation of dibenzoyl disulfide has recently appeared in the literature (8). This is the reaction with triphenyl phosphine and does not lend itself to practical quantitative use:

$$C_6H_5COSSCOC_6H_5 + (C_6H_5)_3P \rightarrow ((C_6H_5)_3P(SCOC_6H_5)_2) \rightarrow$$
$$C_6H_5COSCOC_6H_5 + (C_6H_5)_3PS$$

SUMMARY.

A method is described for the quantitative conversion of dibenzoyl disulfide to benzoic acid by hydrolysis with 40% aqueous potassium hydroxide. Several ineffectual procedures for the quantitative degradation of dibenzoyl disulfide are summarized.

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THE GENUINE CARDIAC GLUCOSIDES.*

BY ARTHUR STOLL.[1]

Those glucosides which constitute the large class of cardiac glucosides, are derived from numerous plants belonging chiefly to the *Liliaceæ*, *Ranunculaceæ*, *Scrophulariaceæ* and *Apocynaceæ*. Several of these poisonous plants such as *Scilla maritima* and Convallaria majalis, Helleborus niger, Adonis vernalis and Nerium oleander, the principal species of Digitalis and Strophanthus, Periploca and Acocanthera and some others have been the subject of more or less profound chemical studies.

In discussing this subject, I shall attempt to deal only with a small part of this vast field of research, and more particularly with some of the more important types of cardiac glucosides, isolated in a pure state and studied in my laboratory. These include the glucosides of *Scilla maritima*, *Digitalis lanata*, *Digitalis purpurea* and *Strophanthus kombé*, all of which are medicinal plants largely employed in therapeutics; one of them, since the most ancient times.

From the chemical point of view the cardiac glucosides are, as is known, composed of an aglucon fraction and a sugar fraction. The aglucon is the real source of the cardiac action, while the sugar fraction determines the solubility of the glucosides in aqueous media.

As shown in the following table, the aglucons of the cardiac glucosides which have been thoroughly studied and analyzed up to the present time, present only slight differences in their chemical composition.

TABLE I.—FORMULAS OF THE AGLUCONS OF THE BETTER KNOWN CARDIO-ACTIVE GLUCOSIDES.

Strophanthidin	$C_{23}H_{32}O_6$
Digitoxigenin	$C_{23}H_{34}O_4$
Gitoxigenin	$C_{23}H_{34}O_5$
Digoxigenin	$C_{23}H_{34}O_6$
Periplogenin	$C_{23}H_{34}O_5$
Sarmentogenin	$C_{23}H_{34}O_5$
Uzarigenin	$C_{23}H_{34}O_4$
Ouabagenin	$C_{23}H_{34}O_8$
Scillaridin A	$C_{24}H_{30}O_2$

In the above tabulation it is interesting to note that *scillaridin A*, the aglucon of the glucoside of *Scilla maritima*, possesses one carbon atom more than the other aglucons.

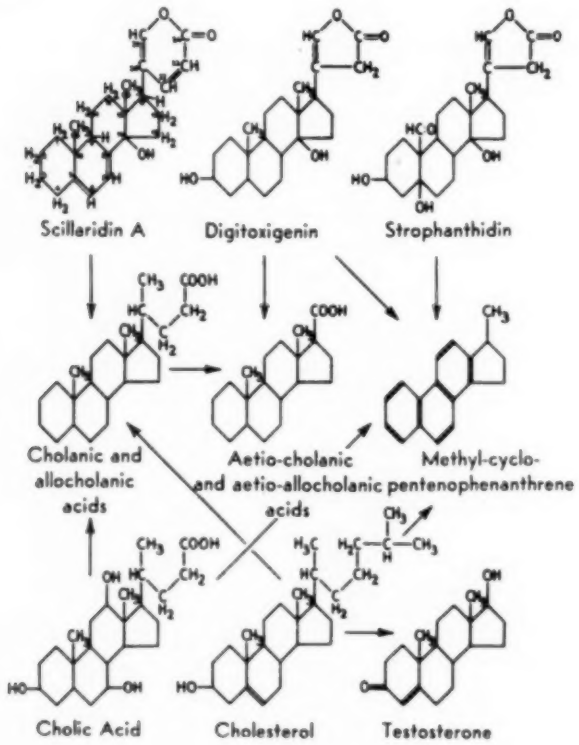
During recent years the study of the constitution of the aglucons of the cardiac glucosides has shown that these substances are related to the large class of the sterols and bile acids and, therefore, have a constitution closely related to the sex hormones. This same class of substances includes also the cardio-active principles of animal origin, such as bufotalin which is a characteristic constituent of toad venom.

* Read before the Department of Pharmacology, University of Chicago, May 24, 1937, on the invitation of Dr. E. M. K. Geiling, Professor of Pharmacology.

[1] Basle, Switzerland.

The relations of the aglucons of cardiac glucosides to the sterols and bile acids have been established by the production of identical degradation products from both groups of substances. Thus Jacobs and Elderfield obtained ætiocholanic acid from digitoxigenin and in a similar way Tschesche degraded uzarigenin to ætio-allocholanic acid. It has further been possible to transform *scillaridin A* by dehydration and, following total hydrogenation, without loss of carbon atoms and without modifying their structural arrangement, into allocholanic acid, which latter also may be obtained from biliary acids by an analogous method. In a very direct and clear way, a glucoside of vegetable origin and the bile acids occurring in animal products, have thus been linked.

TABLE II.—FORMULAS OF SOME DERIVATIVES OF CYCLO-PENTENO-PHENANTHRENE AND THEIR CORRELATIONS.



For purposes of comparison we have completed the above table by the formulas of cholic acid and cholesterol, and have indicated by arrows the chemical transformations that interlink the different members of these groups. All these substances possess a skeleton with 4 condensed carbon rings, the structure typical of cyclopentenophenanthrene. The carbon rings are all completely hydrogenated except where double bonds are indicated.

On closer examination we see that the formulas of digitoxigenin and strophanthidin contain a five-membered lactone nucleus with one double bond, which is typical for the aglucons with 23 carbon atoms. Strophanthidin is further char-

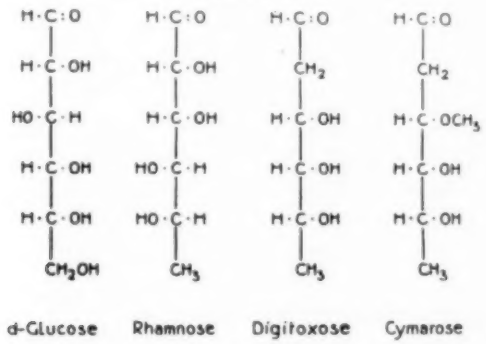
acterized by an aldehyde group attached to carbon atom 10. In *scillaridin A* the lactone nucleus is 6-membered and includes 2 double bonds.

The formulas of the aglucons show the hydroxyl groups to which the sugars are fixed by a glucosidic linkage. In the case of the strophanthins and Digitalis glucosides it is the hydroxyl group, attached to carbon atom 3, which is the carrier of the chain of sugars. In *scillaren A*, we do not know the position of the hydroxyl group which possesses the function of carrying the sugars, because this hydroxyl group, on hydrolysis, is eliminated with formation of a double bond. That is why the structural formula of *scillaridin A* is not yet definitely established.

This brief review of the chemistry of the aglucons, which has been mostly based on the extensive work of W. A. Jacobs and his collaborators, was intended to show the relations of the cardio-active constituents to other natural substances.

The sugars isolated from the cardiac glucosides are either widely occurring, such as *d*-glucose and rhamnose, or sugars specific for the cardiac glucosides, such as digitoxose and cymarose. These latter are characterized by the absence of a hydroxyl group at carbon atom 2 and for this reason they must be considered as 2-deoxysugars.

TABLE III.—SUGARS OF THE CARDIO-ACTIVE GLUCOSIDES.



The modifications undergone by the cardiac glucosides during storage or unsuitable manufacturing processes of the drugs do not, as a rule, concern the aglucon fraction which, with few exceptions, preserves its initial constitution even after successive elimination of the sugar molecules. The modifications of the sugar fraction are of first consideration. Before proceeding further, we must, first of all, define the expression "genuine glucosides." By this we understand the unchanged initial cardiac glucosides as they pre-exist in the fresh plant, carefully dried.

We know that in cardiac therapeutics many physicians prefer the powdered fresh Digitalis leaf to substances which have been isolated from it. In these circumstances, we were, therefore, justified in asking ourselves if the pure products isolated up to then, such as digitoxin or "digitaline cristallisée" and other glucosides obtained from galenical preparations, were different from the cardiac glucosides originally contained in the plant. I may state now that a difference actually exists. We have established in the course of our researches that it is the glycolytic enzymes which play the principal rôle during the transformation of the genuine cardiac glucosides into those previously known.

Biochemistry has shown that the many different chemical reactions of the living cell are achieved by the agency of enzymes, and one may accept that well-directed enzymatic reactions, *i. e.*, those which follow in sequence, and with an intensity appropriate to cellular life, constitute the chief distinctive characteristic, perhaps even the essence of the life of the cell.

The living cell, above all the vegetable cell, possesses special capacities, in view of the synthesis of the most complicated compounds. Thanks to the regulating mechanism of the enzymatic processes, the reactions of disintegration of matter which furnish the energy necessary to vital functions, follow each other gradually, thus making the best use possible of the energy liberated.

After the death of the cell, the enzymatic processes alter entirely. The mechanism controlling the enzymes ceases, the processes of synthesis retrogress and general decomposition begins.

The first important results obtained in the study of enzymes have already shown that the dead but fresh cellular substance, carefully treated, still contains the enzymes which, under appropriate conditions, exercise a hydrolytic action. The proteinases hydrolyze the albumins, the lipases and the esterases hydrolyze the fats, as well as the esters; the glucosidases hydrolyze the polysaccharides and the glucosides. In the living cell, a number of these enzymes may participate in the synthesis of the substances which they subsequently decompose.

In the light of these considerations, we now understand why substances which formerly passed as being genuine substances, are now revealed actually as products decomposed by enzymes. We may cite, in this connection, one of the earliest examples known, that of crystalline chlorophyll which, long considered as a natural product, was shown later to be a product of conversion due to an enzyme, chlorophyllase. This enzyme substitutes ethyl alcohol for the alcohol phytol. We can understand that Nativelle may have thought his crystalline digitalin to be a natural product, this supposition being current until recently. It is only during the past few years that crystalline digitalin has been recognized to be a decomposition product, hydrolyzed by a glycolytic enzyme from a glucoside originally richer in glucose, a genuine glucoside.

Knowledge of the chemistry of enzymatic action has only recently been used to advantage in pharmaceutical chemistry in the preparation of active products from the natural cellular substance. Many years ago Perrot and his school first drew attention to the probable presence of ferments with an oxidizing and diastatic action in certain drugs, belonging chiefly to the Digitalis group; they established that it is not possible to prepare crystalline digitalin from stabilized fresh leaves of Digitalis purpurea.

Later, in 1926, Jacobs and Hoffmann discovered that the seeds of certain varieties of Strophanthus contain a glycolytic enzyme which they called strophanthobiase. Starting from amorphous mixtures of cardiac glucosides isolated from the drugs, they made use of this enzyme to prepare crystalline glucosides with a lower sugar content. These experiments on enzymatic decomposition in the case of Strophanthus kombé, however, did not lead to the isolation of the genuine glucoside in crystalline form. On the other hand Jacobs has given us a typical example of enzymatic decomposition, with the reaction of elimination of a molecule of glucose,

starting from crystalline *k*-strophanthin-β which is transformed into cymarin under the influence of the enzyme. Still, as we now know, *k*-strophanthin-β may itself be derived by enzymatic hydrolysis from a glucoside richer in sugar.

In order to isolate the initial cardiac glucosides we adopted a procedure the reverse of that of the American authors, *i. e.*, we suppressed the action of the enzymes before extraction of the glucosides and thus facilitated the preparation, in a pure state, of the cardiac glucosides as they exist in the natural drug. We then systematically submitted these pure initial cardiac glucosides to hydrolysis by enzymes and by more or less powerful chemical agents. This procedure enabled us to isolate, describe and analyze the products corresponding to all stages of the hydrolysis. Thus were elucidated the relations between the initial glucosides, unknown until then, and the cardiac glucosides already used in therapeutics, all of which were shown to result from enzymatic decomposition.

The first drug treated successfully by our method was *Scilla maritima*. From it we isolated a pure product, two-thirds of which consisted of well-crystallized *scillaren A* (Plate 1), and the remaining third of amorphous, but still more active, *scillaren B*. We observed that *scillaren A* is only obtained in good yield from the bulb of fresh squill if the extraction is carried out very rapidly. If the extract is left in contact with the squill substance the initial *scillaren A* loses, owing to the action of an enzyme, a molecule of glucose, and is transformed into *proscillaridin A*, a well-crystallized product, but with a lower sugar content. My collaborator, Dr. Kreis, has demonstrated that the addition of salts, such as ammonium sulfate, prevents enzymatic action even more effectively than rapid extraction. The added salt causes coagulation of the cellular substance, and prevents completely the action of the enzyme which we have called *scillarenase*. Accordingly, without seeking to destroy the enzyme by drastic measures such as heating, which is damaging to *scillaren A*, we have been able to suppress enzymatic action and to obtain the glucoside in its initial state. Thus the basis for a convenient technical method, which permits the preparation of an initial glucoside in good yield, was created. I do not propose here to enter into more detail regarding the preparation of *scillaren A* and the glucosides of Digitalis and Strophanthus, still to be considered, because these methods are fully described in our experimental publications.

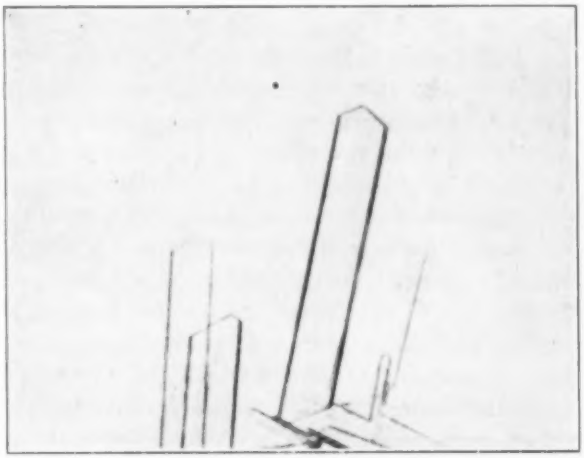
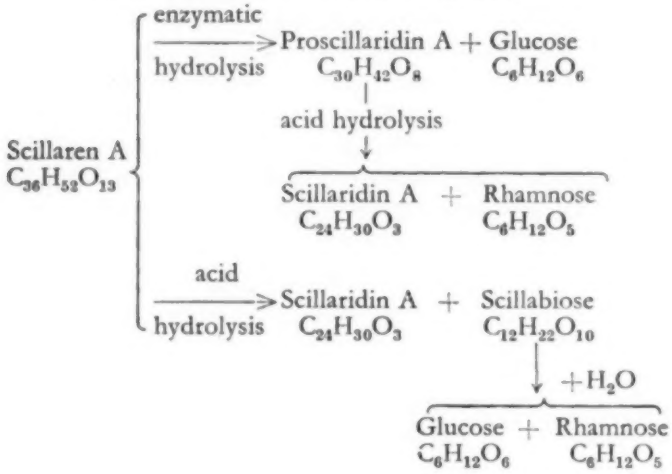


Plate 1.—Scillaren A (from 50% methanol).

Analytical investigations have shown that *scillaren A* is composed of an aglucon, *scillaridin A*, and the sugars, rhamnose and glucose. Table IV illustrates the successive enzymatic and chemical decomposition of the glucosides down to the aglucon.

TABLE IV.—THE HYDROLYSIS OF SCILLAREN A.



Scillarenase splits *scillaren A* into *proscillaridin A* and glucose; acids in their turn hydrolyze this new glucoside, *proscillaridin A*, into *scillaridin A* and rhamnose. The acids attack *scillaren A* at a point different from that of the enzyme, and one may thus obtain, in one step, the aglucon and a sugar, scillabiose, which is then decomposed by prolonged action of the acid into glucose and rhamnose.

Scillaren A is a simple example of a genuine glucoside which an enzyme may decompose under suitable conditions. When we came to apply the experiences gained with squill to Digitalis purpurea, unexpected difficulties were encountered. In the case of this latter species the question was more complicated, the initial cardiac glucosides, obtained by an analogous method, consisting of a mixture of various substances, none of which could be prepared in the crystalline state.

Much more favorable conditions have been encountered in the case of *Digitalis lanata*, a species of Digitalis which has recently enjoyed special favor in cardiotherapy. Having recourse again to the enzyme-inhibitor method in order to avoid the degradation of the glucosides, it was found possible to extract from *Digitalis lanata* a glucosidic complex in the form of beautiful crystals and representing more than half of the total quantity of the glucosides in the leaf. Further investigations showed that this complex to which we gave the name Digilanid (Plate 2) is composed of three separate glucosides, the *digilanids A*, *B* and *C*, which appeared to be crystallographically isomorphous.

The separation of the two components, *a* and *b*, of chlorophyll, realized by a purely physical method, *i. e.*, by fractional separation from a fat solvent and a mixture of alcohol and water, had already presented a serious problem. The separation by analogous methods of these three digilanids, so closely resembling each other in all their properties, was still more complicated. I shall not attempt to describe this method in detail here. It consists in systematic fractionation in non-miscible solvents such as chloroform and aqueous methyl alcohol. More than fifty fractionations were necessary in order to obtain *digilanid B*, the proportion of which is lowest, in a pure state. When the leaves treated come from a good crop, freshly gathered and perfectly stored, the Digilanid obtained consists of about 46%

digilanid A, 17% *digilanid B* and 37% *digilanid C*. It is in these proportions that Digilanid has been introduced into therapeutics and these proportions are maintained strictly constant.

Analytical researches have shown that three different aglucons, digitoxigenin, gitoxigenin and digoxigenin, correspond to the three *digilanids A*, *B* and *C*. In so far as the sugar fraction of their molecules is concerned, the three glucosides have the same constitution. To each of the three aglucons are attached three molecules of digitoxose, a molecule of glucose and an acetyl group. It is a curious fact that this acetyl group determines the isomorphism of the crystals of the three digilanids. If this group is eliminated, which may readily occur when one works without precautions in an alkaline medium, the deacetyldigilanids are obtained, of which only the *deacetyldigilanid C* crystallizes, the other two, *A* and *B*, being amorphous.

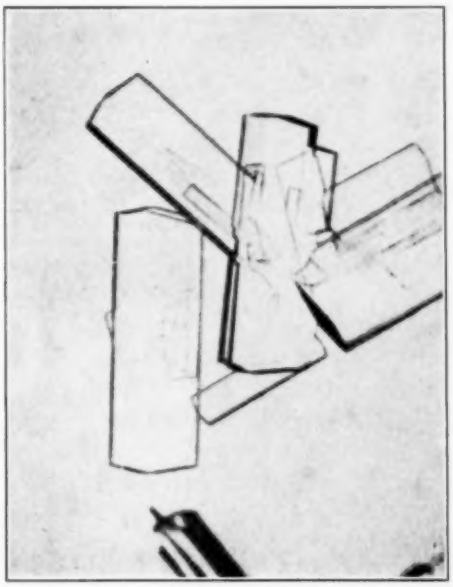


Plate 2.—Digilanid (total glucosides from methanol).

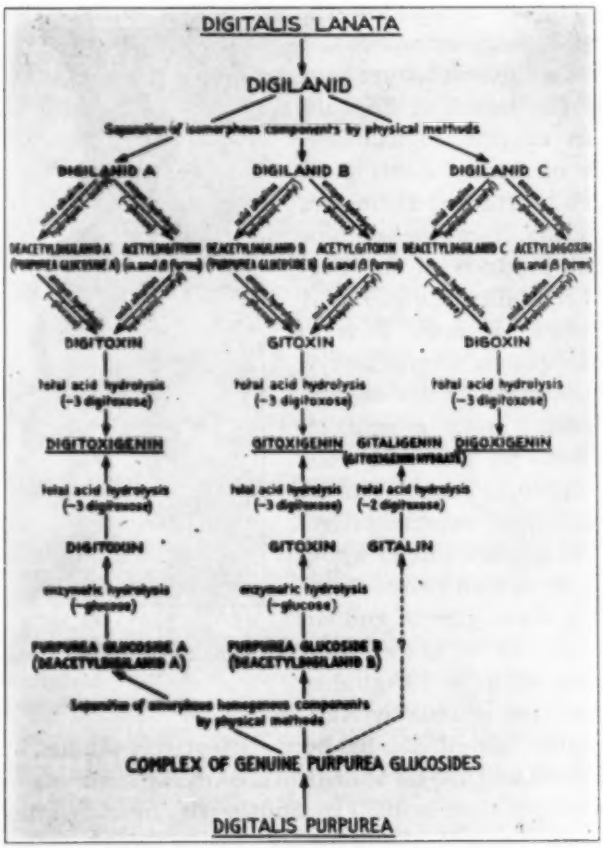
Researches of a different nature have established that the leaves of *Digitalis lanata* contain an enzyme, digilanidase, which is capable of readily splitting off the glucose, which is attached at the end of the chain of sugars, from the "genuine glucosides." The products of this degradation are well crystallized; *digilanid A* gives acetyldigitoxin, *digilanid B* gives acetylgitoxin and *digilanid C* gives acetyldigoxin. Under the mild action of calcium hydroxide the acetyl group is split off in its turn and thus we arrive at what we may call the digitoxin stage, from the name of the principal representative. This is the stage of degradation to which the glucosides of the older digitalis chemistry known as digitoxin, gitoxin and digoxin, correspond. It is known that digitoxin is identical with the "Digitaline crystallisée" discovered in 1869 by Nativelle. This substance, like gitoxin, has been exhaustively studied by Cloetta and by Windaus and his school. In so far as digoxin is concerned, it was isolated from *Digitalis lanata* for the first time in 1930 by Smith, who furnished its description.

As is seen from Table V, the two stages of the process of degradation of the initial glucosides to the glucosides of the digitoxin stage may also be carried out in reverse order, *i. e.*, the acetyl group of the digilanids may be split off first by chemical action and then the glucose fraction of the deacetyldigilanids may be separated by the action of the enzymes. If, then, the hydrolysis is completed by the action of an acid, we obtain in each of the three series, three molecules of digitoxose, plus the corresponding aglucon.

After the chemical relationships between the three most important initial glucosides of *Digitalis lanata* and the known glucosides of the digitoxin stage had thus been clearly determined, an attempt to obtain the initial glucosides of *Digitalis*

purpurea, in a pure state, had greater chance of success. However, the difficulty was appreciably increased here, owing to the small quantity of the glucosides in *Digitalis purpurea* as compared with *Digitalis lanata;* there are also many more secondary substances in the drug of the purpurea species. Finally, the initial glucosides of purpurea have not yet been obtained in a crystalline state. It was necessary for us to perfect the methods of extraction and separation of the glucosides. On the other hand, owing to the number of operations necessary for the purification of the products, the yields were always very small. Nevertheless, it was

TABLE V.—THE INTERRELATIONSHIP OF THE LANATA AND PURPUREA GLUCOSIDES.



eventually possible to isolate two essential principles and to establish that one, the *purpurea glucoside A*, is identical with *deacetyldigilanid A*, and the other, *purpurea glucoside B*, with *deacetyldigilanid B*.

The table shows how these two glucosides are related to the others, and how they are decomposed by the action of digipurpidase, an enzyme present in the drug. The molecule of glucose attached at the end of the chain of sugars, is then readily split off, giving digitoxin and gitoxin. These glucosides, as already mentioned, have been known for a fairly long time, and were first extracted from

Digitalis purpurea. It has not yet been possible to isolate an initial glucoside, corresponding to gitalin, also obtained from *Digitalis purpurea*.

A survey of the various well-defined digitalis glucosides, arranged according to the aglucons and carbohydrate contents, is presented in Table VI. The equation

TABLE VI.—DIGITALIS GLUCOSIDES ARRANGED IN THE ORDER OF THEIR AGLUCON AND THEIR SUGAR CONTENT.

$C_{49}H_{76}O_{19}+5\ H_2O$ Digilanid A	$C_{23}H_{34}O_4+$ Digitoxigenin	$3\ C_6H_{12}O_4$ Digitoxose + $C_6H_{12}O_6$ Glucose + CH_3COOH Acetic acid
$C_{47}H_{74}O_{18}+4\ H_2O$ Deacetyldigilanid A (Purpurea glycoside A)		$3\ C_6H_{12}O_4$ Digitoxose + $C_6H_{12}O_6$ Glucose
$C_{43}H_{66}O_{14}+4\ H_2O$ Acetyldigitoxin (α and β)		$3\ C_6H_{12}O_4$ Digitoxose + CH_3COOH Acetic acid
$C_{41}H_{64}O_{13}+3\ H_2O$ Digitoxin (1871)		$3\ C_6H_{12}O_4$ Digitoxose
$C_{49}H_{76}O_{20}+5\ H_2O$ Digilanid B	$C_{23}H_{34}O_5+$ Gitoxigenin	$3\ C_6H_{12}O_4$ Digitoxose + $C_6H_{12}O_6$ Glucose + CH_3COOH Acetic acid
$C_{47}H_{74}O_{19}+4\ H_2O$ Deacetyldigilanid B (Purpurea glycoside B)		$3\ C_6H_{12}O_4$ Digitoxose + $C_6H_{12}O_6$ Glucose
$C_{43}H_{66}O_{15}+4\ H_2O$ Acetylgitoxin (α and β)		$3\ C_6H_{12}O_4$ Digitoxose + CH_3COOH Acetic acid
$C_{41}H_{64}O_{14}+3\ H_2O$ Gitoxin (1925)		$3\ C_6H_{12}O_4$ Digitoxose
$C_{35}H_{56}O_{12}+2\ H_2O$ Gitalin	$C_{23}H_{36}O_6+$ Gitoxigenin-hydrate	$2\ C_6H_{12}O_4$ Digitoxose
$C_{36}H_{56}O_{14}$ Digitalinum verum	$C_{23}H_{30}O_3+$ Dianhydrogitoxigenin	$C_7H_{14}O_5$ Digitalose + $C_6H_{12}O_6$ Glucose
$C_{49}H_{76}O_{20}+5\ H_2O$ Digilanid C	$C_{23}H_{34}O_5+$ Digoxigenin	$3\ C_6H_{12}O_4$ Digitoxose + $C_6H_{12}O_6$ Glucose + CH_3COOH Acetic acid
$C_{47}H_{74}O_{19}+4\ H_2O$ Deacetyldigilanid C		$3\ C_6H_{12}O_4$ Digitoxose + $C_6H_{12}O_6$ Glucose
$C_{43}H_{66}O_{15}+4\ H_2O$ Acetyldigoxin (α and β)		$3\ C_6H_{12}O_4$ Digitoxose + CH_3COOH Acetic acid
$C_{41}H_{64}O_{14}+3\ H_2O$ Digoxin (1930)		$3\ C_6H_{12}O_4$ Digitoxose

for the complete hydrolysis of each individual glucoside is given, and the large brackets include those groups of glucosides which are derived from the same aglucon, the lowest member of each group corresponding to the digitoxin type.

In comparing the glucosides of the two species of digitalis, it is quickly realized that *Digitalis lanata* represents, from various points of view, a drug of superior

value. That does not mean that the invaluable services which *Digitalis purpurea* has rendered to medicine since Withering introduced it into therapeutics, should be underestimated. But *Digitalis purpurea* possesses only a fraction of the activity of *Digitalis lanata*. Further, this latter species gives three different types of aglucons, all three being present in Digilanid, which makes for synergy in their action. The component C built up with digoxigenin is lacking in *Digitalis purpurea*.

Thanks to the precise analytical study of each of the three *digilanids*, *A*, *B* and *C*, it has been possible to find a quantitative method of analysis for determining the proportions of the three components in the total products. The three constituents of Digilanid, may, therefore, be accurately dosed by weight, thus guaranteeing constancy in composition and action. Digilanid, therefore, not only possesses the total action of the natural drug, but is free from the dangers of the instability and inconstancy of cardioactivity characteristic of *Digitalis purpurea*. The search for an analogous method for determining the proportions of the constituents of the total product obtainable from *Digitalis purpurea* has, up to now, met with insurmountable difficulties. The following shows how easily the glucosides of Digitalis decompose and, consequently, the importance to be attached to their quantitative determination. On extracting, by careful methods, crystalline digilanid from an infusion freshly prepared according to the method of the Swiss Pharmacopœia, only 50% of the Digilanid originally present in the leaves is obtained intact, the other half being decomposed. It is well known that, once prepared, the infusion rapidly loses its activity—in the hands of the patient, so to speak.

After these studies of squill and the two species of Digitalis, it was of great interest to proceed to researches on some important members of the large strophanthus family. As already mentioned, the researches of Jacobs demonstrated that strophanthus seeds contain glycolytic enzymes. It was to be anticipated, therefore, that by suppressing enzyme action prior to extraction, we should find glucosides richer in sugars.

Our first attempts were deceptive. The total glucosidic product extracted from the seeds of *Strophanthus gratus*, gave more than 80% ouabain, a well-crystallized substance known for a very long time, of which the constituents are ouabagenin and a single sugar, rhamnose. The question which still remains unanswered is whether glucosides, richer in sugar, exist in the seeds of *Strophanthus gratus*.

On the other hand, we have been able to extract from the seeds of *Strophanthus kombé* a very beautiful specimen of a genuine glucoside, unknown until now in a pure state. The amorphous mixture of the glucosides of this drug is, as we know, widely used in therapeutics under the name of *k*-strophanthin. Side by side with cymarin, a compound of strophanthidin and cymarose, Jacobs isolated *k*-strophanthin-β, which contains a molecule of glucose more than cymarin. He succeeded in transforming *k*-strophanthin-β into cymarin by splitting off the molecule of glucose, by the action of an enzyme, strophanthobiase.

In the course of experiments recently carried out in our laboratory by Dr. Renz, the seeds of *Strophanthus kombé* have given singularly weak proportions of cymarin and of *k*-strophanthin-β. We have succeeded in extracting from them, in well-crystallized form, a new glucoside representing more than three-fourths of the amorphous mixture of glucosides. It contains one glucose molecule more than *k*-strophanthin-β and was named *k-strophanthosid* (Plate 3). In order to prepare

this new glucoside the essential is to prevent enzymatic glycolysis, but special fractionation processes must be applied in order to obtain it in such a state of purity that it crystallizes.

It will be noted from the above table that *k*-strophanthosid is the glucoside with the largest sugar content.

Among all the known initial cardio-active glucosides *k*-strophanthosid furnishes the most typical example of a degradation by successive stages. Treated with strong acid it decomposes partly into its aglucon, strophanthidin, and partly into a well-crystallized triose until now unknown, strophanthotriose. This triose is composed of a molecule

Plate 3.—*k*-Strophanthosid (from methanol-chloroform).

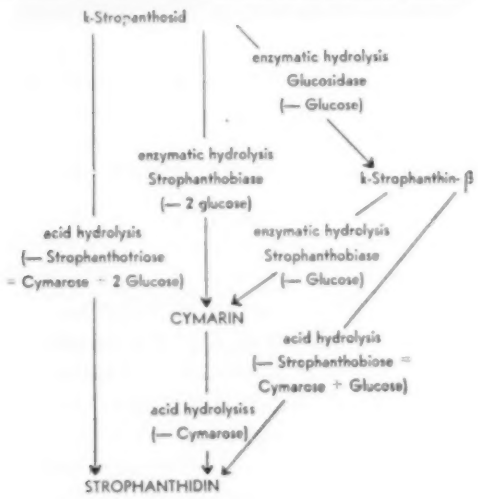
TABLE VII.—STROPHANTHUS GLUCOSIDES AND SOME RELATED CARDIAC GLUCOSIDES.

$C_{30}H_{44}O_9$ Cymarin	$+H_2O$	=	$C_{23}H_{32}O_6$ Strophanthidin	$+C_7H_{14}O_4$ Cymarose
$C_{36}H_{54}O_{14}$ *k*-Strophanthin-β	$+2H_2O$	=	$C_{23}H_{32}O_6$ Strophanthidin	$+C_7H_{14}O_4$ Cymarose $+C_6H_{12}O_6$ Glucose
$C_{30}H_{44}O_9 \cdot (C_6H_{10}O_5)x$ amorphous *k*-Strophanthin	$+(1+x)H_2O$	=	$C_{23}H_{32}O_6$ Strophanthidin	$+C_7H_{14}O_4$ Cymarose $+xC_6H_{12}O_6$ Glucose
$C_{30}H_{44}O_9$ Allo-cymarin	$+H_2O$	=	$C_{23}H_{32}O_6$ Allo-strophanthidin	$+C_7H_{14}O_4$ Cymarose
$C_{30}H_{46}O_8$ Sarmento-cymarin	$+H_2O$	=	$C_{23}H_{34}O_5$ Sarmentogenin	$+C_7H_{14}O_4$ Sarmentose
$C_{30}H_{46}O_8$ Periplo-cymarin	$+H_2O$	=	$C_{23}H_{34}O_5$ Periplogenin	$+C_7H_{14}O_4$ Cymarose
$C_{29}H_{44}O_{12}$ Ouabain	$+H_2O$	=	$C_{23}H_{34}O_8$ (Ouabagenin) (Decomposition, $-H_2O$)	$+C_6H_{12}O_5$ Rhamnose
$C_{30}H_{46}O_9$ Oleandrin	$+H_2O$	=	$C_{23}H_{34}O_5$ (Gitoxigenin?) (Decomposition) $-2H_2O$ = Digitaligenin	$+C_7H_{14}O_5$ Digitalose?
$C_{35}H_{54}O_{14}$ Uzarin	$+2H_2O$	=	$C_{23}H_{34}O_4$ (Uzarigenin) (Decomposition, $-H_2O$)	$+2C_6H_{12}O_6$ Glucose
$C_{36}H_{52}O_{13}$ Scillaren A	$+H_2O$	=	$C_{24}H_{30}O_3$ Scillaridin A	$+C_6H_{12}O_5$ Rhamnose $+C_6H_{12}O_6$ Glucose
$C_{30}H_{42}O_8$ Proscillaridin A		=	$C_{24}H_{30}O_3$ Scillaridin A	$+C_6H_{12}O_5$ Rhamnose

of cymarose and two molecules of glucose. It gives quantitatively these three sugars when submitted to strong acid action.

If *k-strophanthosid* is subjected to the action of the enzyme of Strophanthus two molecules of glucose are eliminated, and cymarin is obtained, which decomposes into strophanthidin and cymarose on acid hydrolysis. This enzymatic cleavage is similar to one already performed by Jacobs with the amorphous mixtures of strophanthus glucosides, but now starts with a pure crystalline substance. If, on the other hand, *k*-strophanthosid is acted upon by the *a*-glucosidase of yeast, a single molecule of glucose is split off and *k*-strophanthin-β is obtained. This splitting off of a molecule of glucose, under the action of *a*-glucosidase, proves that this molecule, situated at the end of the chain, is fixed in the form of *a*-glucose. Under the action of strophanthobiase *k*-strophanthin-β gives cymarin, and by direct acid hydrolysis it gives strophanthobiose and strophanthidin.

TABLE VIII.—HYDROLYSES OF K-STROPANTHOSID.



The series of successive degradations of *k*-strophanthosid shows in a striking manner to what numerous risks of hydrolytic degradation a genuine cardio-active glucoside is exposed, if special precautions are not taken in the storage and treatment of the drug. In addition to the enzymes and the natural acids of the plant, capable of exercising a hydrolytic degrading action, there exists also other kinds of injurious enzymes. Thus Jacobs has found, in the seeds of *Strophanthus kombé*, an enzyme which has the effect of isomerizing the aglucon part after the seeds have been ground. By slow extraction Jacobs obtained, instead of cymarin, allocymarin, which is practically inactive.

When the amorphous mixture of glucosides of *Strophanthus kombé* is utilized in therapeutics, it is necessary to reckon with the manifold transformations which are always possible. One may now eliminate these hazards, thanks to the discovery of *k*-strophanthosid, a well-crystallized substance which represents more than three-quarters of the glucoside content of the drug.

It is only during the last few months that it has been possible to extract *k-strophanthosid* from *Strophanthus kombé*, and to isolate it in a pure state. A pharmacologic study of this substance now in progress has already demonstrated its very great activity. Clinical testing of the new product has been undertaken, but some years must pass before we can formulate a definite opinion as to its therapeutic value. At all events, it offers to the experimenter one advantage, that of being an absolutely pure substance, capable of exact dosage and always constant in activity. As with any new medicament, it is necessary to guard against forming an opinion too hastily.

The following table (IX) gives a view of the activity of some of the cardio-active

glucosides that we have discussed. These values, which have served as a starting point for clinical investigation, are the result of the extensive pharmacologic researches of Professor E. Rothlin.

TABLE IX.—TOXICITY OF DIGITALIS GLUCOSIDES.

Glucoside.	Frog (Medium Lethal Dose, Sub-Cut. Inj., Timeless Method). Frog Units per Mg.	Cat (Intravenous Infusion According to Hatcher). Cat Unit = Mg. per Kg.
Digilanid (total complex)	620	0.343
Digilanid A	690	0.380
Digilanid B	540	0.400
Digilanid C	640	0.281
Purpurea-glucoside A	690	0.368
Purpurea-glucoside B	315	0.369
Digitalin cryst.	400	0.420
Digoxin	650	0.280
k-Strophanthosid	1850	0.126
Cymarin	1500	0.146
Ouabain (g-Strophanthin)	2400	0.100
Scillaren A	1200	0.145

Without entering into further detail, I wish to emphasize the considerable difference in toxicity between the Digitalis glucosides on the one hand and the strophanthins on the other. The values in frog units and cat units show parallel variations from one glucoside to another. Nevertheless, the proportion is far from being constant, which shows once more the importance of a profound clinical study of the pure glucosides.

Like the physician, the biochemist knows that, with the preparation and the clinical study of the medicament, the essential work is far from complete. Cardiac diseases are so diverse in origin, and the reaction of the patient is so individual that even to-day, when there is available a series of valuable cardiotonics, the essential value of a treatment still depends upon the art of the physician. In every case it is necessary to choose carefully the medicament and the dosage best suited, but medical treatment is facilitated if the physician has at his disposal cardiotonics of constant activity, and as complete in action as possible.

The objects in biochemical research on drugs are not simply and purely scientific; there is not only the question of determining the constitution and the chemical relationships of the various, physiologically interesting substances. Such researches also have a practical significance, since their aim is to place the contribution of chemical science in the hands of the physician.

CONCLUSION.

This discussion has dealt with attempts to isolate the active principles of drugs in pure form without destroying their natural initial state. Only a few examples in the very specialized and limited field of cardiac glucosides have been given. There are doubtless many other cases where the genuine active principles of drugs are not yet known and, therefore, a vast field for investigation still remains.

DECOMPOSITION OF CITRIC ACID BY FERRIC IRON.*

BY S. I. PELTZ AND E. V. LYNN.[1]

It is a well-known fact that many preparations of iron undergo decomposition when exposed to light. This is particularly true of those containing quinine and strychnine (I. Q. S.). Although some of the used solutions of iron are stable, the problem of possible deterioration and of means to prevent it has long been a challenge to the pharmacist.

The best known method for avoiding such changes is to exclude the light, a simple procedure but one not always completely practicable. With only partial protection, the rate of changes is roughly proportional to the intensity of light, but eventually the preparation alters in color, evolves gas or deposits muddy or crystalline precipitates; possibly all three of these take place simultaneously in the same solution.

All of the solutions which decompose in this way contain ferric iron and some salt of an organic acid. Indeed, these two factors seem to be the exclusive ones, although secondary changes may occur subsequently.

Many of the numerous papers which have appeared on this subject are entirely empirical. In order to prepare stable solutions of iron, some have added various reagents, others have furnished an excess of acid or have nearly neutralized, while still others have altered the methods of preparation or have suggested many other schemes, all without substantiated reasons for so doing. Practically all of these proposals have been tried unsuccessfully. This literature is well summarized by Burt (9). Scientific investigations of the subject are very few and much of the present evidence is insufficient and even contradictory.

It is known that oxidation of citric acid will give rise to carbon dioxide, acetone and other volatile products. This may take place under the influence of heat and manganese dioxide (1), of sunlight and uranic oxide (2, 3), or of sunlight or ultraviolet and ferric compounds (4, 6, 7, 8, 9), or of oxygen and light (5). The nature of the products in each case has never been adequately investigated and much of the past or present surmises are conflicting.

The more specific changes which follow reaction of ferric salts and citric acid are largely matters of conjecture. Using an ultraviolet (mercury arc) lamp, Benrath (7) found that acetone and formaldehyde are formed, together with hydrocyanic acid and nitrous oxide from the ferric nitrate used. Mueller (8) found that ferric iron is reduced to ferrous in the sunlight and that carbon dioxide is produced. Burt (9) confirmed these results and obtained the iodoform test for acetone after distilling an exposed solution. He also decided that three molecules of carbon dioxide are produced for each molecule of acetone and formulated the reaction as

$$C_6H_8O_7 + O \rightarrow C_3H_6O + 3CO_2 + H_2O$$

We were able to confirm the formation of carbon dioxide and to establish that it is the only gaseous product. Flasks containing 2.5 Gm. of citric acid in 50 cc. of water and 0.25 Gm. of ferric hydroxide were connected to potash absorption bulbs and exposed to sunlight. When all evidence of reaction had ceased, the bulbs

* Presented before the Scientific Section, A. PH. A., Minneapolis meeting, 1938

[1] Professor, Massachusetts College of Pharmacy.

were found to have increased in weight by 0.075 ± 0.0005 Gm. Separately collected samples of the gas were completely absorbed by potash in a Hempel pipette.

Besides evolution of gas, the only distinct change is disappearance of the brown ferric hydroxide. Where there is sufficient of the latter to start with, it is only reduced in amount. Careful examination also shows that the originally colorless solution is now very slightly greenish yellow and contains ferrous but not ferric ions, as shown by tests with ferricyanide and thiocyanate. After standing away from sunlight for a short time but exposed to the air, the almost colorless solution gradually acquires a darker greenish tinge. This is probably brought about by direct oxidation in the air, as is experienced with many ferrous solutions. Exposure to sunlight always results in removing the color and tests for ferric iron.

Neither acetone nor formaldehyde could be identified in the final solution. The experiments of Burt could be duplicated, but his assumption that acetone is formed seems to be erroneous. The residual solution gave no iodoform and no color with alkaline sodium nitroprusside (Rothera or Legal). Distillation gave a neutral liquid which responded to the iodoform reaction, as Burt had shown, but no nitroprusside test. Furthermore no oxime could be obtained from the first distillate. Tests for formaldehyde in either liquid were negative.

The exact combination of iron in the decomposed solution was not discovered. After removal of the iron by hydrogen sulfide, which was easily accomplished contrary to Burt's experience, and evaporation of excess sulfide, ether failed to extract significant amounts from the acidified solution, although it will remove appreciable quantities of citric acid from its aqueous solution. On the other hand, a calcium salt was readily formed by precipitation and this was found to contain 31.05 per cent of CaO as compared with 33.73 per cent from normal calcium citrate. Also, portions of the original ferrous liquid, after evaporation and ignition, gave 29.15 per cent of ferric oxide, as compared with 30.76 per cent from normal ferrous citrate. Acetates and oxalates could not be identified.

Finally it was determined that neutral citrates will not decompose with ferric hydroxide in strong sunlight. The iron goes into solution as might be expected, but none of it was found in the ferrous state. In galenicals which contain citrates and do deteriorate, we may assume primary formation of free acid by hydrolysis or otherwise.

SUMMARY.

1. Citric acid is at least partially decomposed by ferric hydroxide in the sunlight to give carbon dioxide and a soluble ferrous salt, probably a citrate. Alkali citrates do not decompose under the same conditions.

2. No acetone and no formaldehyde can be detected in the final solution. A substance is found in a distillate which gives the iodoform reaction but no nitroprusside test.

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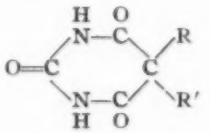
CROTYL SUBSTITUTED BARBITURIC ACID DERIVATIVES.*

BY EDWARD E. SWANSON[1] AND WILLIAM E. FRY.[1]

In a previous communication (1), it was observed that there is obvious relationship between the pharmacological action and the chemical structure of certain barbituric acid derivatives. In the primary or secondary alkyl substituted compounds, with an increase in the number of C-atoms in the alkyl group, both the minimal anesthetic dose (M. A. D.) and the minimal lethal dose (M. L. D.) grow relatively smaller, but when the alkyl radical is longer than 5 C-atoms, the amount required to produce anesthesia or death in rats again increases. As the alkyl chain lengthens, the therapeutic index, or ratio between M. L. D. and M. A. D., appears to be gradually greater. The duration of action becomes shorter. More recently, it has been reported that the substitution of a methyl or an ethyl group on the nitrogen (nitrogen alkyl substituted barbituric acid derivatives) (2), or the substitution of an allyl or methallyl (2-methyl-allyl) (3) on one of the 5-5 positions, or a sulfur atom (4) in place of the 2 C-atom obviously reduces the duration of action. This shorter duration of action is independent of the quantity of drug administered.

The present investigation deals with the study of a number of new crotyl (3-methyl-allyl) substituted barbituric acid derivatives synthesized by Doran and Shonle (5), with the general formula:



wherein R-alkyl radical may be a primary or secondary alkyl radical with 2 to 5 C-atoms; and R′, a crotyl (3-methyl-allyl) radical.

Albino rats weighing 80 to 125 Gm. (average 99 Gm.) were used in this study. Solutions of the sodium salts of the compounds were injected intraperitoneally. The M. A. D., the duration of action, and the M. L. D. were determined by using 5 animals for each dose level.

As shown in Table I, these barbituric acid derivatives have a much shorter duration of action. Thus, the substitution of a crotyl (3-methyl-allyl), similar to the nitrogen alkyl barbituric acids and methallyl (2-methyl-allyl) compounds, produces a change (shorter) in the duration of action. Compound number 6, Crotyl-*n*-butyl-thio barbituric acid, shows convulsions with little or no hypnotic or anesthetic properties.

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* Presented before the Scientific Section, A. PH. A., Minneapolis meeting, 1938.

[1] From the Lilly Research Laboratories, Indianapolis, Indiana.

TABLE I.—COMPARISON OF THE PHARMACOLOGIC ACTION OF 10 CROTYL SUBSTITUTED BARBITURIC ACID DERIVATIVES.

No. of Compound.	Barbituric Acids (Crotyls).	No. of Rats.	M. A. D. Mg. per Kg.	Average Duration of M. A. D. Min.	M. L. D. Mg. per Kg.	M. L. D. / M. A. D.
1	Cis-crotyl-ethyl	50	100	372	280	2.80
2	Trans-crotyl-ethyl	40	100	300	240	2.40
3	Crotyl-*n*-propyl	60	130	120	340	2.60
4	Crotyl-iso-propyl	54	70	200	180	2.57
5	Crotyl-*n*-butyl	64	110	40	320	2.90
6	Crotyl-*n*-butyl-thio	15	*	...	...	...
7	Crotyl-sec-butyl	54	80	120	220	2.75
8	Crotyl-iso-butyl	55	100	45	300	3.00
9	Crotyl-iso-amyl	36	120	40	180	1.50
10	Crotyl-sec-amyl	51	90	66	200	2.22

No. of Compound.	Barbituric Acids (Parent Compound).	No. of Rats.	M. A. D. Mg. per Kg.	Average Duration of M. A. D. Min.	M. L. D. Mg. per Kg.	M. L. D. / M. A. D.
1						
2	Ethyl-ethyl	39	340	1400	480	1.41
3	Ethyl-*n*-propyl	49	150	1140	210	1.40
4	Ethyl-iso-propyl	27	170	1520	220	1.37
5	Ethyl-*n*-butyl	40	80	450	200	2.44
6	.....	..	...	...	...	...
7	Ethyl-sec-butyl	35	60	600	130	2.16
8	Ethyl-iso-butyl	35	120	540	220	1.83
9	Ethyl-iso-amyl	60	80	210	200	2.50
10	Ethyl-sec-amyl	27	50	200	120	2.40

* Convulsions.

CONCLUSIONS.

1. A number of crotyl (3-methyl-allyl) barbituric acid derivatives have been synthesized and studied pharmacologically.

2. The substitution of a crotyl radical in barbituric acid derivatives distinctly shortens the duration of action.

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NATIONAL ASSOCIATION OF RETAIL DRUGGISTS.

At the Sherman Hotel, on October 10th, the N. A. R. D. will hold its fortieth annual convention. Among the speakers will be: Congressman Wright Patman, of Texas; Senator John E. Miller, of Arkansas; and Commissioner of Narcotics, H. J. Anslinger. It is expected that three thousand druggists will attend, and "Nothing is being left undone to really make this event long remembered in the history of drugdom."

PROBLEMS ENCOUNTERED IN PROMOTING THE USE OF OFFICIAL PRODUCTS.*

MARVIN J. ANDREWS.[1]

It is apparent, from the number of requests for information received by the U. S. P. and N. F. Publicity Committee of Maryland from interested parties outside of the state, that many other similar organizations are encouraging dentists and physicians to write more prescriptions. Although we have published several articles on this subject, which have appeared in the JOURNAL OF THE AMERICAN PHARMACEUTICAL ASSOCIATION (1), it is our purpose at this time to note a few of the difficulties that may be encountered in promoting the use of the official products. It will be necessary to criticize the work of our own committee, as well as the work of other committees, both local and national. Our object is to help groups who are just starting as well as those who are conducting programs.

The Selection of a Committee.—The selection of the personnel of any committee is a very important step. The president of any organization should give much time and thought to appointing the members of a U. S. P. and N. F. Publicity Committee or of an Interprofessional Relations Committee; above all he should not appoint men on the basis of friendship. Each member of the committee should be capable, energetic and practical. The chairman, if possible, should be a member of the teaching staff of a school of pharmacy; the next best person would be a progressive professional pharmacist. The other members of the committee should be retail pharmacists who stand high in professional circles, are available for meetings and at the same time are congenial with other members of the committee.

Financing the Program.—After the committee has been appointed and tentative plans have been made for its activities, the next step is to obtain sufficient funds to carry out the proposed plan. This is a usual stumbling block, but if the committee applies itself diligently and persistently, some plan to finance the program can usually be worked out.

The method will vary according to locality; so I shall mention only a very few of the many ways of obtaining the necessary funds.

1. The state of local associations supply the necessary funds from membership dues or finance the program by special assessment.

2. In case the associations are not financially able to provide the necessary funds, an effort should be made to obtain a dollar from each retail drug store in the city, county or state in which the program is to be carried on.

3. If the second method proves unsuccessful, the Committee should try to obtain larger donations from a smaller number of interested persons. A great deal can be accomplished if twenty-five or thirty interested stores will contribute $10.00 each and charge it off to advertising. If this plan is used, the stores contributing should be given all the credit.

4. Having obtained some definite results, it is then possible to contact other professions and invite them to defray a portion of the expense. The success of this

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* Presented before the Section on Practical Pharmacy and Dispensing, A. PH. A., Minneapolis meeting, 1938.

[1] Assistant Professor of Pharmacy, School of Pharmacy, University of Maryland.

method will necessarily depend upon the interest of the other professions in the project.

The accepted plan will be governed by the amount of money available. To be successful, the program must be placed on an educational basis.

Methods of Promoting Prescription Writing.—There are many ways to stimulate members of the dental and medical professions to write more prescriptions. As our medical schools devote very little time to the teaching of the various methods of writing prescriptions, the graduates know little or nothing about writing a prescription. The committee should take advantage of the great many opportunities for coöperation presented by these circumstances.

By using the drugs and preparations contained in the U. S. P. and the N. F. as the ingredients in the suggested prescriptions, the Committee has the primary requirement for successful results: a worthy product. The U. S. P. and the N. F. are recognized by the Federal Pure Food and Drug Act and by the laws of the various states as the legal standards for drugs and preparations used in this country. Likewise, approximately 90 per cent of all the drugs and preparations included in *Useful Drugs* published by the American Medical Association, also those mentioned in the leading books on therapeutics, are official in the U. S. P. and N. F.

I can see no reason for comparing the prices of the official products with those of nationally advertised products containing essentially the same ingredients. Although the official products are much cheaper, it is impossible for any committee to control the price of prescriptions. With this point in mind, I feel sure that all will agree that a campaign based on price alone will have a short life. On the contrary, a campaign conducted on an educational basis not only will be helpful to the dentist and the physician, but also will gain their respect and coöperation.

There are many methods that may be used to stimulate the dentist or physician to write prescriptions. Among these are scientific displays, personal contacts and written propaganda.

Scientific Displays.—A great deal of time and thought is required in the preparation of a scientific display that will make a lasting impression. The display should be arranged to present a definite story and not include everything contained in both the U. S. P. and the N. F. The type of display will depend upon many things, the most important of which are the space allowed, the financial set-up, and the nature of the group to whom it is to be presented.

For a major exhibit, the Committee will be expected to prepare a display on a budget of two or three hundred dollars to compete with similar displays prepared by individual commercial concerns at a cost of two or three thousand dollars. Likewise, it will have to prepare the entire display within two or three weeks. With these considerations in mind it is interesting to compare the two displays. The commercial concern features only a few products neatly displayed with very few signs. Descriptive material is presented in pamphlet form and is distributed by well-trained attendants. On the other hand the typical booth prepared by a Committee is usually smaller; yet it contains a great number of different drugs and preparations. These are described by large signs, in front of which are displayed bottles or jars containing the compounded prescriptions. In most instances the attendant is out looking over the other booths instead of remaining at his own.

By using photographs of two booths prepared by the same professional group,

I hope to illustrate contrasts in the use of displays. The first is a display built around a single topic with five signs of three different heights and a sufficient number of suggested prescriptions, all within the eye range of a person of normal height. The result is a very neat and impressive display. The second display is built around seventeen different therapeutic headings in a space suitable for only three or four topics at most. In addition to the center display there are thirty-four large signs, eleven of which extend from the floor to the top of a counter about thirty inches high. These lower signs are impossible to read and also handicap the efficiency of the booth.

When pharmaceutical associations are arranging for scientific displays before dental or medical groups, they should endeavor to obtain as much space as possible in a desirable location. A desirable location is essential as the number of visitors to the booth will be in proportion to the number that pass by. Likewise, a wide shallow booth is preferable to a narrow deep booth for the former type is much more effective for display and also accommodates more visitors.

The selection of material will depend upon whether it is being prepared by a pharmaceutical group alone or in conjunction with a dental or medical group. In case the pharmaceutical group is to work alone, it is best to select a pharmaceutical subject, such as vehicles. An excellent display can be made by illustrating the use of incorrect and correct vehicles for certain drugs, or by illustrating the various forms in which a single drug can be dispensed.

Personal Contacts.—It is not practical for a small pharmaceutical association or group to employ a so-called detail man to call upon physicians and dentists, for the value received would never equal the amount expended. Each visit by the detail man would cost the association approximately one dollar. For illustration, let us use a group of 1500 physicians, 500 dentists and 500 pharmacists. A single detail man working full time would not be able to make more than one visit a year to each physician and dentist. This plan would cost each pharmacist four dollars; yet the individual store would receive very little credit for the expenditure. Then, again, annual visits are of very little value in a publicity campaign.

It is difficult to suggest a better method, yet I feel it is best for some representative group to sponsor the written material and have the retail pharmacist follow up the work by a personal visit to the physician or dentist.

Written Propaganda.—Different associations or groups send out various forms of written propaganda, among which are blotters, leaflets, bulletins, letters or cards of various sizes. Each medium has its advantages and disadvantages. I shall not take time to discuss their relative merits except to say that the form adopted should be of permanent rather than of transient value.

The object of such propaganda is to stimulate dentists and physicians to write prescriptions that indicate the correct medicament and dose for the individual patient. As a result they will find it necessary to write an individual prescription for each patient. A committee should present its suggested prescriptions in such a way that they will serve as illustrations of the correct methods of writing prescriptions; it should not expect the dentist or physician to copy the exact combination. This viewpoint eliminates the type of publicity that includes only stereotyped prescriptions, as this type is of little value in stimulating a dentist or a physician to write the prescriptions best suited for his patients.

In general, written propaganda should present the following information:

1. The various combinations of drugs used for a particular disease. If the suggested prescriptions are taken from an authority and are quoted exactly, a note should give the originator credit, at the same time transferring the responsibility for its therapeutic accuracy from the Committee. If the prescription is not quoted, then a foot-note should be made, *e. g.*, "The dose in these prescriptions should be adjusted to suit the patient." This statement implies that the dose should be determined by the prescribing dentist or physician.

2. The various ways in which a single drug may be prescribed. This purpose is accomplished by writing suggested prescriptions for a powder, a capsule, a liquid preparation, etc. In addition to the different types of pharmaceutical preparations in which a single drug may be prescribed, the physical appearance of any one form may be changed by using different vehicles or different added coloring.

3. Vehicles. In case a single vehicle is selected for discussion the following information should be given whenever possible: official titles, flavor, color, alcoholic content, reaction to litmus, uses and incompatibilities.

4. General Information. As the heading implies, this is the topic under which are discussed such items as: Latin terms used in prescriptions, apothecaries' weights and measures with their equivalents, coloring agents used in prescriptions, etc.

Next I shall consider some of the many criticisms I have heard in reference to written propaganda issued by local, state and national committees.

1. The printed or mimeographed copies are not clear. A few cents difference in price may mean a waste of money. The copy must be legible if you expect members of other professions to read or use the material.

2. The propaganda is not suitable for filing. This was one of the chief objections made to our first bulletins before we changed to our present 3 x 5-inch cards. Last year when we sent out an inquiry in reference to supplying missing cards, we were very much surprised to find that only a few physicians needed replacements.

3. The propaganda contains only stereotyped prescriptions. In most instances the value of the suggested prescriptions lies not only in that they are written correctly, but also in the fact that they remind the prescriber that the same ingredients can be prescribed in many different ways. The practical pharmaceutical information given on the card is the reason why a great many dentists and physicians become interested in the propaganda and follow every issue.

4. The variation in nomenclature used for the ingredients contained in the prescription. Whichever official nomenclature is selected, whether Latin, English or abbreviated Latin, it should be used throughout the prescription. Mixing the nomenclature or giving the wrong abbreviation is a reflection upon the committee and indicates that they are careless or that they are not familiar with the products they are endeavoring to promote. The number of physicians and dentists that notice this one point is surprising. In Maryland we use the official abbreviated Latin titles. This is done to get away from the long Latin titles and case endings, and also to prevent the patient from reading the prescriptions, as he will try to do if it is written in English. The use of abbreviated Latin tends to reduce self-medication and other forms of lay medication.

5. The quantities of the ingredients contained in the suggested prescriptions should be practical. The suggested quantities may be given as a single dose with directions for making a definite number of such doses or the total quantities may be given for the entire prescription. In either case the quantities should be given in both the Metric and Apothecary systems. If the conversion is not exact, the approximate equivalent should be used with a note at the bottom of the card, such as "Conversions from Metric to Apothecary are approximate and not exact." This takes care of those prescribers who use only the Metric system as well as those who use only the Apothecary system.

6. The directions to the pharmacist are not clear. The suggested Latin terms or abbreviations should be those in common use. It is always wise to be practical and not inject theoretical ideas.

7. The ingredients in the suggested prescriptions are not compatible. This is often the case when the combinations are taken from textbooks. The best policy is always to test the prescriptions by allowing the compounds to stand for several days. In many instances the theoretically perfect prescriptions prove to be dismal failures when they are compounded.

8. The pharmacists do not stock the ingredients contained in the prescriptions. This is often the case when rare drugs or chemicals are suggested. This phase of the work should be scrutinized very carefully by the retail pharmacists on the committee.

I shall conclude my discussion with the most important point: coöperation. In work of this kind it is essential to have the coöperation of the retail pharmacist as he is the one who fills the suggested prescriptions. Likewise, if the campaign is conducted on an effective educational basis, the committee will receive the cooperation not only of the dentists and physicians but also of the detail men and the salesmen of all the reputable pharmaceutical manufacturing companies. The success of our campaign in Maryland is best indicated by the fact that many of the little index boxes we recently prepared have been sold to dentists, physicians and pharmacists by salesmen representing commercial concerns. Last, but not least, we feel proud of our efforts in Maryland as the little green filing box, containing an index and all cards issued to date and bearing the inscription "℞ using U. S. P. & N. F. Preparations," is no longer a local affair but has been found to be useful in thirty-eight other states, as well as Canada.

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KANSAS STATE BOARD OF PHARMACY.

Regulation 15. A regulation to clarify and give support to Section one (Section 65–1601, R. S. 1923) of the pharmacy law of the state of Kansas, to prevent a registered pharmacist from devoting part time to a drug store not having any other registered assistance:

It shall hereafter be unlawful for anyone to conduct a drug store within the state of Kansas unless such store is supervised by at least one registered pharmacist, registered in the state of Kansas; said pharmacist to devote full time to one store when there is no other registered pharmacist to be used as a substitute or for relief of the supervising pharmacist.

The penalty for the violation of Section one (Section 65–1601, R. S. 1923) of the pharmacy law shall apply to and for the violation of regulation 15.

DISCOLORATION OF AROMATIC SPIRIT OF AMMONIA.*

BY C. C. REED,[1] P. L. BURRIN[1] AND F. E. BIBBINS.[1]

Aromatic spirit of ammonia has been used extensively in the practice of medicine for the last few centuries. When it is diluted sufficiently with water, aromatic spirit of ammonia, due to its reflex action and palatability, has been used chiefly to correct the hyperacidity of the stomach, more especially when accompanied by nausea or sick headache. Early records indicate that this preparation was recognized first officially in the London Pharmacopœia of 1721 under the name of *Spiritus Salis Volatilis Oleosus* (1). Shortly afterward this name was changed to *Spiritus Ammoniæ Aromaticus*. Since then various modifications have been suggested in the method of manufacture and in the formula from time to time, but the present American formula has been in use for a number of years without any change.

The fact that this product discolors readily is indicated by the following description given in the U. S. P. XI for aromatic spirit of ammonia: "a nearly colorless liquid when freshly prepared, but gradually acquiring a yellow color on standing." Since discoloration may be indicative of some change that has taken place in the galenical preparation subsequent to manufacture, it was thought desirable to investigate the possibilities of overcoming such a tendency. Upon making a review of the literature, very little could be found about discoloration, or methods to overcome it. Various methods of storage have been suggested to overcome this tendency, and the present U. S. P. has incorporated some of these ideas, giving instructions to preserve the spirit in glass-stoppered bottles in a cool place protected from light.

Maisch (2), in view of the fact that essential oils were not the only volatile constituents of plants, suggested the continuation of making the spirit by distillation from the drugs (same as U. S. P. 1840 procedure) since by following such a procedure the appearance was improved. A. Gertrude Flanders (3), after experimenting on a number of different pharmacopœial processes including suggested modifications for the preparation of this spirit, concluded that distillation was necessary in order to obtain a colorless spirit.

In the seventh revision of the U. S. P., oil of myristica was substituted for the oil of pimenta to prevent the tendency to darken (4), and since that time the formula has not been changed.

Thresh (5), some fifty-five years ago, proposed to avoid the distillation of the ammonium carbonate in making this preparation. The present British Pharmacopœia directs that this spirit be made by the same procedure. The amount of oils distilled by such a method is not definite and this offers a primary objection to the formula. The method has an advantage in the fact that a spirit made in such a manner will not discolor readily, although it will change color in time (6). Seward (7) suggested a modification of the method of the British Pharmacopœia of 1885. He recommended introducing less water into the still, distilling slowly and thereby securing all of the modified spirit in the distillate.

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* Presented before the Section on Practical Pharmacy and Dispensing, A. PH. A., Minneapolis meeting, 1938.

[1] From the Control Laboratories, Eli Lilly and Company, Indianapolis.

Pollard (8) suggested still another modification. He proposed to avoid the distillation of the alcohol, and instead, use the distillation of the oils with water to obtain the first portion of the product, rejecting certain fractions toward the last, the presence of which he maintained would impair the delicate aroma.

It was the opinion of the authors that the terpene content of the oil of lemon might be a possible factor in the discoloration of the spirit upon aging. Accordingly, several experiments were set up for comparison, based upon the terpene content of the oil of lemon, using the various oils which could be purchased on the open market, *i. e.*, oil of lemon, Sicilian, U. S. P., oil of lemon cold pressed Californian, U. S. P., and oil of lemon (terpeneless), the latter containing not less than 60 per cent citral. The citral content of the various oils of lemon was determined by the assay method outlined in the U. S. P. IX. The following table gives the resulting data:

		% Citral By Weight.
1.	Oil of lemon, U. S. P. (Sicilian)	4.84
2.	Oil of lemon, U. S. P. (Sicilian)	4.32
3.	Oil of lemon cold pressed Californian, U. S. P.	2.62
4.	Oil of lemon (terpeneless)	71.10

By preparing aromatic spirit of ammonia from the above oils, and calculating the equivalent amounts, based on the citral content of the oil of lemon, the following results were obtained:

Experiment Number.	Procedure.	Oil of Lemon Used.	Results after 30 Days' Aging.	Results after 60 Days' Aging.	Results after 120 Days' Aging.
1.	U. S. P. XI	No. 2	Slight color	Slight color	Slight color
2.	U. S. P. XI	No. 2	Slight color	Slight color	Slight color
3.	U. S. P. XI	No. 4	Trace	Trace	Trace
4.	U. S. P. XI	No. 3	Slight color	Slight color	Slight color
5.	B. P.	No. 2	Colorless	Colorless	Trace

Several things were noticed in making the above experiments. Spirit No. 3 was free from haziness when first made; consequently the rate of filtration was rapid and easy. Spirits No. 1 and No. 2 prepared following U. S. P. XI procedures were cloudy when finished, and required the aid of a filtering medium to clarify the finished product. This necessitated slower filtration, with the possible loss of ammonia. In following the instructions of the British Pharmacopœia in making experiment No. 5 some difficulty was encountered, as only 820 cc. of distillate could be obtained absolutely clear, whereas the British Pharmacopœia directs that 875 cc. of clear distillate be obtained. After 820 cc. of clear distillate had been obtained and held separately, the next distillate started to become milky as it came through the condenser, and a gradual rise in temperature occurred. However, the milky distillate was collected until the necessary volume was obtained, *i. e.*, 110 cc. The ammonium carbonate and the strong solution of ammonia were added and dissolved in this 110-cc. portion with subsequent filtration. This filtrate was added to the reserve of 820 cc. and enough distilled water added to make 1000 cc.

A second series of experiments was made in order that the results of the first series might be checked. The results are given in the following table:

Experiment No.	Procedure.	Oil of Lemon Used.	Results after 30 Days' Aging.	Results after 90 Days' Aging.
6.	U. S. P. XI	No. 2	Slight color	Slight color
7.	U. S. P. XI	No. 2	Slight color	Slight color
8.	U. S. P. XI	No. 4	Trace	Trace
9.	B. P.	No. 2	Colorless	Very slight
10.	U. S. P. XI	No. 3	Slight color	Slight color
11.	U. S. P. XI	No. 1	Slight color	Slight color

All of the experiments made by the U. S. P. XI procedure fell within the assay standards given, while those made according to the British Pharmacopœia were just under the lower limits. The following formula, the authors believe, will give a product which is equivalent to one produced by the U. S. P. XI method with the added advantages of easy filtration and of developing less color upon aging:

Ammonium carbonate, in translucent pieces	34.000 Gm.
Ammonia water	90.000 cc.
Oil of lemon (terpeneless)	0.667 cc.
Oil of lavender	1.000 cc.
Oil of myristica	1.000 cc.
Alcohol	700.000 cc.
Water, Dist. *q. s.* to make	1000.000 cc.

Follow directions given in the U. S. P. for making the spirit.

CONCLUSIONS.

1. Aromatic spirit of ammonia made by distillation does not discolor as readily as one made by simple solution, thereby confirming previous investigations.

2. A spirit made in accordance with the U. S. P. XI directions, but modifying the formula to use an equivalent amount of oil of lemon (terpeneless), will develop less color upon aging.

3. A spirit made using terpeneless oil of lemon is water-clear and can be filtered rapidly without danger of loss of volatile constituents.

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THE VALUE OF THE HOSPITAL TO THE PHARMACIST.*

BY DON A. BROOKE.[1]

Last year at our New York meeting an interesting paper was presented on the "Value of the Pharmacist to the Hospital."

* Presented before the Sub-Section on Hospital Pharmacy, A. PH. A., Minneapolis meeting, 1938.

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As a retail rather than as a hospital pharmacist I wish to present a short article upon the value of the hospital to the pharmacist and of the opportunity the hospital may afford for the advancement of the profession of Pharmacy.

Of course in the cities and the larger hospitals a full-time pharmacist is nearly always included in the organization but in the smaller communities there are many well-equipped and accredited hospitals which do not have the services of a full-time pharmacist. This is due largely to economic reasons and because of the fact that these hospitals do not have enough work for a full-time pharmacist.

However in such a community the hospital is nearly always the local health center and common meeting place of the leading physicians and surgeons. Most of these hospitals have their prescriptions filled at some local drug store and have the more common solutions made up in surgery. In such a hospital, a qualified pharmacist working in coöperation with the hospital can not only be of real benefit to the institution but can also advance the profession of Pharmacy, both to the allied professions and to the laity.

The first job, of course, is to convince those in charge of the hospital that they need a pharmacist for supervision in making solutions and that it will not raise the overhead costs to the hospital.

Where there is a nurses' training school in connection with the hospital, they are usually very grateful to have a pharmacist take over the class in "Drugs and Solutions" and "Materia Medica" as neither the supervisors nor staff doctors care to teach these subjects. While teaching does take time and study, there is no better way to keep up in drug therapy than to devote two hours per week to teaching.

Personally, I have learned a lot more about the therapy and dosage of drugs from teaching than in my four years in college. Teaching this course also gives the graduating nurses a much higher respect for the profession of Pharmacy and a realization that a drug store can and should be more than a merchandising market or a variety store.

But more important than the nursing school are the monthly staff meetings of the doctors connected with the hospital. In the smaller cities, most of the physicians and often the dentists are staff members and attend these meetings more or less regularly. From the teaching staff it is a short step to secure a place on the monthly staff program where a short talk can be given on drug therapy both official and proprietary.

Now anyone in retail Pharmacy can tell you of the advantages of detail work in building up a profitable prescription practice and anyone who has had experience in detailing doctors knows of the long waits that are unavoidable if you are to see the best prescribing doctors and make a personal call.

However, these staff meetings give the pharmacist a chance every month to personally contact the leading doctors and give information on the newer aspects of drug therapy.

During the two years I have been doing this work I have written up a drug outline for each meeting and given every one of the attending members a copy. Each time I aim to cover as completely as possible a related class of drug therapy. For example, on anti-anemic preparations I try to give an unbiased statement as to the potency and relative cost of the preparations for anemia, by each of the leading manufacturers.

Naturally in giving an outline on such preparations as cough remedies, the emphasis is placed on the official products. At each meeting there is usually a general discussion as to the relative merits of proprietary preparations and a qualified pharmacist can be of real service in this connection.

There is no reason why a doctor should be getting most of his drug information from the detail man who is out to sell his own particular line and naturally will make more or less biased statements. Moreover, the detail men are not going to stress any official preparations but rather encourage the doctors to prescribe ready-made prescriptions. It is this drifting toward ready-made proprietaries that has given many doctors the idea that Pharmacy consists mostly of pouring from one bottle to another.

In this respect the hospital pharmacist probably has a better chance than anyone else to educate the doctors in the use of official preparations and I have found that the physicians themselves are grateful for constructive information on prescription writing.

In my opinion the future of professional Pharmacy lies not so much in passing more laws or raising educational standards as it is in the attitude of the pharmacists themselves toward Pharmacy.

Don't let the community forget that you are a professional person, and the hospital is undoubtedly one of the best places for the doctors, the dentists, the pharmacists and the nurses to meet in a professional way.

THE HOSPITAL PHARMACY.*

HAROLD A. GRIMM.[1]

Pharmacy, as a profession, has established itself as an essential part of hospital service, taking its place of importance among other major departments in our modern institutions. Twenty years ago it was not customary for hospitals to employ pharmacists. On the other hand many hospitals did not then employ pathologists, radiologists or dietitians, personnel which to-day are to be found in practically all hospitals of fifty beds and upwards.

Assuming that there was a neighborhood drug store to which the hospital could send its drug baskets, prescriptions and requisitions, the loss of time and general inconvenience of such an arrangement would make the plan most unpopular with staff and hospital personnel alike.

Emergencies arise, the attending physician is making rounds and wants to change the medication, or anyone of several other situations common to all hospitals may develop, which make it imperative that there be easily and quickly available a standard stock of drugs and biologicals. Obviously, then, the individual nursing units themselves must be adequately supplied with the necessities, and the use of the corner drug store as a substitute for the hospital pharmacy is not practical.

We may safely say, therefore, that the modern hospital needs a modern pharmacy, in charge of a competent pharmacist. The department should be centrally

* Presented before the Sub-Section on Hospital Pharmacy, A. PH. A., Minneapolis meeting, 1938.

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located, easily accessible, well lighted and ventilated and be of sufficient size to meet the demands to be put upon it.

Too seldom do hospital architects give proper consideration to the need for storage space of bulk drugs, space for manufacturing stock solutions and shelf space. In those hospitals whose size justifies the purchase of drugs in barrels and drums, bulk storage in the pharmacy itself may be impractical, yet the savings in drug costs over a period of years will more than pay for the space occupied.

The equipment of the hospital pharmacy is important. Instead of soda fountains and luncheonettes, the hospital pharmacy will be more likely to require an analytical balance, burettes, volumetric flasks and other scientific apparatus. Under the heading of "essentials," too, should be listed a good torsion balance, a refrigerator of ample size, water still, an alcohol vault and a narcotic safe. In some hospitals, tablet machines, filter apparatus, suppository molds and a steam sterilizer may be necessary, depending upon the kind and amount of manufacturing to be done. If there were a need for it, a mixing machine might be added and used to advantage in making ointments and emulsions, but this will not apply in the average hospital.

Depending again upon the size of the institution and the amount of space required for the pharmacy, it should be located in the most accessible place consistent with the use to which it will be put. We would hardly expect to carry on very extensive manufacturing procedures in a pharmacy located on the main corridor near the main entrance. Yet, for the convenience of patients, hospital employees and visitors, such a location would have definite merit, particularly if the pharmacy was to carry a stock of toilet preparations, magazines, cigarettes, candy, etc., for which there is a great demand.

The hospital pharmacy provides an excellent field for the woman pharmacist, particularly the type who is interested in scientific pharmacy. She must be a teacher, since nurses, interns and staff doctors will consult her frequently, seeking information and advice. She must be alert to changes that are taking place, to new drugs, their action and dosage. She should know prices and be able to estimate the probable demand for a new drug, regulating the volume of her purchases accordingly. Many drugs prove to be of only temporary popularity and it is both expensive and embarrassing to be left with a lot of dead stock.

With the help of a committee from the medical staff, appointed for that purpose, the pharmacist should be responsible for compiling the Hospital Formulary, this to contain a list of drugs and formulas that are considered to be suitable for use in the Out Patient Department as well as for stock items in the medicine cabinets of the nursing units. If the hospital has a Standing Order Book, care must be exercised to include such drugs as are mentioned in it and conversely, the Standing Order Book should make good use of the Formulary. When properly set up and in operation, this makes for greater simplicity in manufacturing, helps to keep inventories down and improves service.

From time to time the pharmacist should inspect the drug cabinets in the nursing units. Soiled labels and broken stoppers detract from the appearance of neatness and orderliness that hospitals so constantly strive for. On the other hand neatly lettered labels, applied with a coat of protective varnish, not only help appearances but inspire confidence and both are essential.

It is important that biologicals kept in the refrigerators of the nursing units be checked periodically to be sure that the stock is fresh. In an emergency, when these products mean so much to the patient there must be an adequate supply that is dependable.

In the smaller institutions the pharmacist may be of great help to the Administrator in the matter of purchasing surgical supplies such as sutures, cotton and gauze as well as rubber goods, glassware, syringes and needles. Chemicals for use by the laboratory and X-ray department might well be a part of the pharmacy stock since the pharmacist in many instances will be called upon to make up reagents and solutions for use in these departments.

More and more is being expected of hospitals and it is not an uncommon occurrence to have a patient go home supplied with drugs for his immediate needs as well as dressings. There are times, too, when they need items of enamel ware, syringes or other sick room supplies. To have such things for sale in the pharmacy relieves the hospital of the problem of having equipment removed or loaned from nursing units, and at the same time serves as a great convenience to the patient and the doctor.

With the knowledge that hospitals provide an excellent field of employment for the pharmacist, it would seem advisable for the student to learn something about the hospital's needs and what is likely to be expected of him. To that end, the school of pharmacy could, without much trouble, give the student an opportunity to learn more of the hospital, its equipment, its services and their relationship with the department in which he is preparing to work.

For the pharmacist who plans to work in a hospital, actual experience in the form of an internship would be most ideal. Such a program would appeal to the hospital Administrator, and at the same time lend encouragement to the scientific aspect of pharmacy, helping to maintain it on a professional basis.

Progress in the field of hospital pharmacy is likely to take a new direction shortly. In New York State, pharmacists employed by hospitals have been invited to become members of the State Hospital Association and a fair number have done so. At the 1938 convention of the ASSOCIATION pharmacists had a prominent place on the program, giving evidence that they as well as other department heads can derive benefit from an exchange of ideas, all to the end that the patients in hospitals may be served most effectively and intelligently.

MANUFACTURING IN THE HOSPITAL PHARMACY.*

I. T. REAMER.[1]

In a paper recently published in the JOURNAL OF THE AMERICAN PHARMACEUTICAL ASSOCIATION entitled "Medical Requirements of the Hospital Pharmacy," by Dr. W. J. Stainsby, the following paragraph was printed, "I feel that the pharmacist to be successful should, from time to time, critically examine the various preparations he issues to the hospital for the purpose of determining whether they

* Presented before the Sub-Section on Hospital Pharmacy, A. PH. A., Minneapolis meeting, 1938.

[1] Pharmacist, Duke Hospital, Durham, N. C.

can be simplified or improved, or whether or not he can manufacture them cheaper or better than they can be obtained commercially." I believe that every hospital pharmacist should have the above statement typed and placed on the wall of his office, so that he will be reminded continually of one of his most important functions.

From time to time we hear of, or read about the lack of interest in the pharmacy from the viewpoint of the superintendent. Inadequate equipment, improper working space and salaries, all seem to be a part of the routine complaints of a large group of hospital pharmacists. I believe that these problems could be eliminated or at least improved if more attention would be paid to the manufacture of pharmaceuticals.

The best method of attack is to tabulate the cost of the commercial preparations and compare this list with a record of the cost of products manufactured in the pharmacy. Follow this up by making a list of products which you could manufacture if more space, equipment and help were available. I have done this on several occasions and the difference in the cost figures of the commercial preparations and the manufactured products is amazing. If you want to get ideas on the preparations which could be made, make an effort to visit other hospital pharmacies. The larger teaching institutions are preferable because of the amount of work which they must handle and the necessity of working on limited budgets due to the large percentage of charity work generally done.

Most hospitals take advantage of the opportunity that they have in buying tax-free alcohol to manufacture U. S. P. and N. F. preparations. It is surprising though that quite a few simple preparations which they can easily make are purchased from commercial manufacturers.

Tablets of sodium chloride for both compresses and intravenous use are bought by many hospitals. A compress solution can easily be prepared of 18% sodium chloride and it may be sent to the wards in quart bottles and the labels marked to read, "dilute 1–20 to make physiological salt solution." If the metric system is in use in your hospital the marking could be, "dilute 50 cc. to 1000 cc. to make physiological salt solution." If sodium chloride is wanted for intravenous use, it can be bought in bulk containers and the amounts wanted to make your solution can easily be weighed on the balances in the pharmacy.

Lubricating jelly can be prepared of a good quality from a simple formula of tragacanth, glycerin, water and some antiseptic such as phenol. Large size collapsible tubes of 7 oz. capacity can be easily sterilized and filled with the jelly lubricant. The saving at our hospital amounts to more than $350.00 per year on this preparation.

Mandelic acid therapy has been accepted during the past two years by the medical profession and working from a formula published in the Jour A. Ph. A. by Dr. Fantus; we made a preparation of our own which has been very satisfactory. The estimated economy over a two-year period of making this preparation has been over $1000.00.

Sometimes when we desire to make certain products we find that the proper equipment is not available. My plans to make our cold cream and to work out a new hand cream formula several years ago were frustrated when I realized that the proper mixers were not present. Upon investigating the equipment used in the

hospital kitchen, I found an electric mixer quite suitable for my purpose. The same condition may be present in other institutions so a visit to your kitchen may prove valuable.

Time is an important factor in manufacturing and preparations should be made as far in advance as it is convenient to do so. We believe that we save time in manufacturing our mouth wash by making 3–5-gallon bottles of concentrated mouth wash at one time. The ingredients are adjusted so that half a gallon of the concentrate will make five gallons of finished product. With this method the three bottles represent one hundred and fifty gallons of mouth wash. Of course if space and large storage tanks are available, another system of preparation might be preferable.

The manufacture of sterile solutions undoubtedly represents the greatest economy that can be effected in the hospital pharmacy to-day. Many preparations other than the routine saline, dextrose, procaine and molar lactate can be prepared. The recently accepted vitamins such as thiamin chloride, cevitamic acid and nicotinic acid should be added to the long list of hospital pharmacy sterile solutions which the progressive pharmacist prepares for his hospital.

A practical plan for helping the hospital pharmacist in his manufacturing would be for the Sub-Section on Hospital Pharmacy to edit an annual booklet of workable formulas. The complete directions for making the products could be listed under each formula. If the institutional pharmacists increase the number of products manufactured in the pharmacy they can easily prove the saving accomplished, and if properly managed the result will be a more wholesome respect for pharmacy and pharmacists.

PUBLIC HEALTH AND SOME HOSPITAL PHARMACIES.*

BY MORRIS DAUER.[1]

The prime duty of society toward its members is the protection of their health as far as is humanly possible. Culture, habits of industry, correct attitudes in social relationships, adequate knowledge of social, historic and political backgrounds, a wholesome interest in and understanding of one's environment; all these are desirable goals of society, but even greater than these is the cultivation and the protection of health, "Mens Sana in Corpora Sano" (a sound mind and sound body).

It is interesting to note in the annals of mankind the steady progress that has been made in our lives; cultural, political, financial and scientific. As man continues in his tasks and daily work toward that ultimate goal of civilization which is perfection, he pauses at different eras long enough to give him a chance to take inventory and appreciate that which has gone before him. The advocates of Technocracy demand in one phase of their study that the machine age exerts an inhibitory force so that man will be able to appreciably adjust all his faculties gradually and in such proportion as to accommodate all changes.

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With the progress of scientific healing, changes occurred to the extent that most branches of the healing art have been definitely defined, and each branch demands specialists who have had the proper training to perform special tasks in the best manner possible. It is to the credit of the American hospitals and to the various organizations which they represent that these plans have been carefully followed, and we find most departments manned by a personnel which is specifically trained in its own particular field to the ultimate advantage of our sick people. It is unfortunate, however, that this plan is not very faithfully adhered to with reference to the compounding and dispensing of medicines and drugs which are given to hospital patients to assist and safeguard their recovery.

Pharmacy has come down through the ages as a distinct and separate branch of the healing art and has been defined "as the art and practice of preparing, compounding, preserving and dispensing medicines to be used in the treatment of the sick." As such, it has been scientifically developed and with such a degree of precision as to greatly assist in the treatment of the sick.

In most civilized countries various laws and acts have been passed and enforced so that public health will not be endangered. The State of New York has rendered yeoman service by being the first state to pass sufficient legislation of a practical and thorough nature to safeguard the interests of public health and professional pharmacists in their pursuit of the very fine and exacting work which they have rendered. Before one can be admitted to the legal practice of Pharmacy, certain educational requirements, with sufficient subsequent practical training, are required. The courses given in the Colleges of Pharmacy are thoroughly supervised by the authorities.

Only those who are properly qualified may be entrusted to prepare medicine for the sick. This rigid supervision, followed by constant inspection, has done much to raise the standing and usefulness of the Pharmacy to the community; and infractions of any degree are punishable by revocation of license, a penalty, which as evidenced by statistics, very few engaged in pharmacy have been called upon to pay.

It does not seem reasonable, in the light of this knowledge, that the same strict adherence to these safeguards of public health is not paid to pharmacies or drug departments which are part of hospitals. Supervision of these pharmacies is left to those in charge of the hospital.

Many surveys have been made of the hospitals throughout the United States and the percentage of those that entrust the important work of compounding and dispensing of medicines to a pharmacist whose professional conduct is supervised by state authorities. Most of these hospital pharmacies are operated by interns and nurses who are so overworked with other professional duties that it is impossible to expect of them the same degree of careful dispensing that we may expect from a trained, licensed pharmacist. This is evidenced from time to time in the public press by the abuses resulting from this practice. In the light of present knowledge and in the interest of public health, legislation should be enacted which will compel all hospitals to employ at least one pharmacist who is licensed in their respective state to assume full charge and responsibility for the compounding and dispensing of medicines; the same as required of those engaged in private practice.

The compounding and dispensing of medicines in a hospital is just as impor-

tant and technical as in the drug store to which a doctor's prescription is brought for compounding. Poisons have to be delicately measured and weighed, poisonous dosages have to be carefully checked and unpalatable drugs must be elegantly compounded with suitable aromatics and flavoring to render them more palatable. Are not the sick in the hospital entitled to the same legal and human care as the sick in their own homes? It is readily admitted, even by those who advocate differently, that we cannot expect the best when the compounding and dispensing is done by anyone except a well-trained pharmacist.

Institutions and hospitals that do not employ licensed pharmacists, but allow their pharmaceutical operations to be carried on by unlicensed and untrained help, do so obviously because of real or alleged economic necessity. Avoidable errors are constantly being made and very often assume such large proportions that at one stroke lives may be needlessly wasted. News items of the daily press bear this out.

It is economically, morally and ethically unsound for any hospital to permit unlicensed pharmacists and others to attend to drug dispensing:

1. Economic. In hospitals which do not employ licensed pharmacists, galenicals, ointments, surgical supplies, cotton, bandages, gauze, etc., are purchased in bulk quantities, usually altogether out of proportion to their needs, and there is much waste due to spoilage, improper handling, improper dispensing and poor storage. A licensed pharmacist can manufacture all galenical and pharmaceutical preparations much cheaper than they can be purchased outside and in the normal amounts needed for use, thereby assuring medicines of official strength and potency at a lower cost and thus automatically eliminating waste. Pharmacists, also, are better acquainted with the market value of drugs, chemicals, etc., and are instrumental in saving money for the institution in this way; they are also trained to assay drugs and chemicals purchased, to assure remedies of proper potency and to detect adulteration.

2. Morally. Patients who are treated at their homes are guaranteed by the laws of the state in which they reside that their prescriptions will be compounded by a pharmacist whose training and integrity have been vouched for by the state. Patients in hospitals where dispensing is done haphazardly by non-pharmacists are not accorded this protection. We must conceive that in hospital practice both medical and surgical patients constantly require the administration of drugs, the nature of which are more potent and vary in form and use from the ordinary remedies which may be prescribed for the ambulatory patients, and these should be compounded and dispensed by those who have met the minimum requirements that the state demands of one to practice Pharmacy.

3. Ethically. Pharmacy as practiced to-day in the modern hospital is a specialized field. The extemporaneous preparation of Fresh Solutions for intravenous medication properly prepared are preferable to ready-made articles purchased in quantity and probably stored for a period; such duties rightfully belong to the realm of pharmaceutical practice.

In conclusion the writer recommends:

(*a*) That in addition to all other requirements for the registration of a hospital, the American Hospital Association and American College of Surgeons require that a hospital be equipped with a pharmaceutical laboratory, the size of which should be

in proportion to the needs of the hospital, as recommended and approved by the Section on Hospital Pharmacy of the AMERICAN PHARMACEUTICAL ASSOCIATION, and that such pharmacy should be under the immediate and personal supervision of a pharmacist licensed in the state in which the hospital is situated.

(*b*) That the AMERICAN PHARMACEUTICAL ASSOCIATION recommend that the State Departments of Health amend their public health laws so that it shall become mandatory for all hospitals to employ only registered pharmacists in the same capacity as they are employed in the retail pharmacy.

(*c*) That the AMERICAN PHARMACEUTICAL ASSOCIATION divide the United States into districts and assign a committee of members of the Sub-Section on Hospital Pharmacy to make periodic inspections, and such committee report in writing, together with recommendations for the approval or disapproval of such hospital pharmacy, and that such recommendations be forwarded by the AMERICAN PHARMACEUTICAL ASSOCIATION to the American College of Surgeons and American Hospital Association for their action in this matter.

(*d*) That the State Boards of Pharmacy shall be empowered to make their periodic inspections and enforce these regulations together with all their other regulations.

(*e*) That the AMERICAN PHARMACEUTICAL ASSOCIATION appoint committees to study this problem at length and make further recommendations.

EXAMINATIONS IN CHEMISTRY.*

BY EDWARD KREMERS.

During a long life time I have not presumed to dictate to my younger asso ciates on the instructional staff how they were to teach or conduct their classes. As a member of a State Board for several years, I have equally refrained from telling my colleagues on the Board how they should conduct their examinations. I have asked for the privilege to conduct my teaching and my examining in accordance with my own views. Having been granted that privilege, I deemed it but right and proper to accord the same privilege to others, no matter how divergent our views on the subject. In accordance with these principles I am to-day subjecting to your criticism a series of State Board examination questions, with the hope that a free discussion thereof may result beneficially to myself as well as others.

Possibly, I should preface my presentation with a few personal remarks. As a student, I have always been willing to do my duty by any subject required of me, be it irregular French verbs, or Kebler's laws in astronomy. But I greatly disliked examinations. As a mere lad, I would get up at sunrise and study Latin or Greek declinations and conjugations. Likewise, I uncomplainingly crammed zoölogical classification from the textbook, though I should have preferred to collect animals, and acquired a knowledge of zoölogical systematics by handling animals as I did, *e. g.*, with beetles. Examinations, however, as already stated, I detested. Hence, at the close of my junior year at the Philadelphia College of Pharmacy, when every-

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thing depended on the final examination, I took a nap before going to the college whereas my roommates crammed for the test. As a senior at Wisconsin, I spent from three to five hours every evening rewriting my lecture notes with the aid of several treatises on the subject. As a result, all I had to do for the fortnightly quiz, was to reread my notes once, whereas my classmates made hard work of "bucking." Even for the doctorate examination at Göettingen I could not persuade myself to cram. True, I did not get a "summa cum laude" but I did not care for the label attached to my degree. I had gone abroad, for knowledge it is true, but primarily for the inspiration that came from such teachers as Kekulé, Wallach, Strassburger and Schimper.

I deemed it desirable to preface my remarks with these personal statements, since what I have to say is naturally influenced by my personality.

I fully realize the difficulty of teaching students in large classes, but large classes we should strive to abolish. I also realize the strain under which an instructor labors when his teaching activity is judged so largely by the percentages of excellents, goods, etc., his class can boast of, or the number of his students who pass the State Board examinations, no matter how vicious such examinations may be. I can appreciate all of these difficulties from a life-long experience. But in the long run, the instructor will not serve himself, much less his students, by compromising his ideals as teacher with the demands of his superiors or the clamors of so-called "practical" members of his profession.

The papers submitted will have to speak for themselves. A few remarks, however, may lead to a better understanding of them.

1. A certain amount of memory work is necessary in every branch of study. Unfortunately, memorizing is not infrequently employed as a substitute for acquiring knowledge. Cramming quiz compends is one thing. Knowledge acquired by observation and doing is a very different matter. Hence in each of the examinations, I have supplied the candidates with a mimeographed copy of two monographs from the U. S. P. or N. F., one inorganic, the other organic. Moreover, I have refrained from selecting complex chemicals, but have chosen simple ones.

The object of a State Board examination is not to ascertain how many facts the candidate has memorized, but to find out whether he "is safe." One of the best tests to ascertain this is to have him show that he can read his Pharmacopœia intelligently. As an aid to the candidate, each monograph is supplied with from half a dozen to a dozen questions, emphasizing points to be interpreted or explained. Finally, the candidate is given an opportunity to write all he knows about the chemicals under consideration. In order to reduce the mental strain as much as possible, but one written examination is given each of the four days. Three hours during the forenoon, are allowed for each written test. Moreover, these written tests are supplemented by a 3-hr. oral examination on the papers.

Now, what have been the results of this experience?

If the objective of the teacher of Chemistry is to teach, not chemicals, but Chemistry, so the objective of the chemical examiner is to ascertain whether the candidate can apply his knowledge of Chemistry, not necessarily of chemicals, in his professional work. To teach the properties of U. S. P. and N. F. chemicals, or even of the latest synthetic new remedies, is not necessarily Chemistry in its best

sense. Unless the candidate has grasped the spirit of Chemistry, his detailed factual knowledge of the latest new remedy may fail him when a newer one appears in his prescription practice.

A comprehensive knowledge of the subject, even if acquired at college, should be supplemented by a study of application in chemical industry. Thus the student may learn to apply the test for iodate in an iodide, but this is little better than mere book knowledge unless he knows something about the process of manufacture that necessitates the introduction of such a test in the U. S. P. True, not all students can visit a chemical factory in which potassium iodide is made. But out of numerous groups of candidates, not one had visited a gas works, a distillery, a tannery, etc. As a result one candidate stated that ammonia was obtained as a product of decomposition of proteins—book knowledge—but did not know that the bulk of commercial ammonia is obtained as a by-product in either gas works or coke works. Not one out of ten knew what malt is. An equally small proportion had seen a lime kiln, hence had only a book knowledge of the preparation of calcium oxide from calcium carbonate (limestone, marble, calcite, etc.). Not many more knew the difference between slaked lime (lime water) and air-slaked lime (plaster). Equally deplorable was their lack of knowledge of the different forms of natural calcium carbonate (limestone and dolomitic limestone, marl, stalactites and stalacmites, calcite (incl. Iceland spar) and aragonite), although they lived in the very midst of these rock formations and minerals and the industries based upon them.

Some of the candidates wrote about ions and electrons: had crammed an electron definition of valence but had no significance of valence itself.

College graduates, who had had a course in volumetric analysis, had no proper conception of a factor, hence made all kinds of mistakes when asked to explain a paragraph dealing with the volumetric determination of, *e. g.*, ammonia. Even more shocking was the failure to state in simple terms the meaning of percentage.

Hence the problem, "If the U. S. P. states that 10 cc. of ammonia water should not yield more than 0.003 Gm. of residue, what percentage of impurity is permissible?" resulted in the greatest variety of answers.

Now who is to blame? The candidate not so much as his teacher. State Board examiners have blamed college teachers that they do not teach their students sufficient Pharmaceutical Arithmetic. They do. But this elementary school task would be quite unnecessary if the grammar school teacher had done her duty. Unfortunately, the college teacher is only too apt to follow the methods of the grammar school teacher. It does not require many years of experience to find out that if a candidate has studied the "Pharmaceutical Arithmetic" by X he can pass satisfactorily an examination based on that text. However, if the examiner takes his questions from the "Pharmaceutical Arithmetic" of Y or Z the candidate is apt to fail. Yet the rules in all three texts may be the same. However, no sooner is a problem worded somewhat differently than the average candidate fails, as in the ridiculously simple test stated above.

Indeed, so simple is this problem that I was tempted to try it out on others than candidates for a Board examination. *First*, I submitted it to an ex-teacher of mathematics. She was stumped and pleaded ignorance of Chemistry. When I pointed out to her that no Chemistry was involved, her husband agreed with me. The second person was a college graduate who had majored in English and now

holds a position of responsibility in a large department store requiring frequent computations. She also failed. The third person was also a college graduate, but she had majored in mathematics. She made a mess of it.

In all three instances, I cared less about a correct answer than about the method of approach. So simple is the problem that, with a realization of the meaning of the word percentage, neither addition nor subtraction, division nor multiplication, the stumbling blocks even of expert mathematicians, need be involved. Yet all three tried to follow a rule, but failed to apply it successfully. Had they forgotten their rules and applied a modicum of reasoning they could not have gone wrong.

It is this failure to apply reasoning that is responsible for so much of our failure in education. If the teacher and examiner are satisfied with memorizing, what else can we expect of student and candidate?

What applies to Arithmetic, applies equally to Chemistry. In the simple statement of the U. S. P. on the volumetric estimation of NH_3 in ammonia water, with the actual factor given, most candidates could not give a rational explanation of its derivation. The answer given, they could not utilize the simple chemical equation, quantitatively interpreted, to show how it was derived.

We hear much these days about comprehensive examinations, a final cramming course, as a college president recently termed the latest fad in pedagogy. Yet with a whole page of U. S. P. text, and a dozen suggestions in the form of questions, few candidates will write more than fifteen to twenty lines for an essay of the subject under consideration. True, some will come with the smart Alec trick and use the words of the U. S. P. text slightly rearranged. But even when subdivisions of the topic were suggested, this aid to the candidate proved of little avail. Again something is radically wrong with our method of teaching if our graduates do not know how to express themselves. Also, State Board questions for fifty years have contributed nothing to this capacity on the part of candidates.

STATISTICS OF INTEREST TO PHARMACY.*

BY H. C. CHRISTENSEN[1] AND LILLIAN H. BOWEN.

At the 1935 N. A. B. P. convention in Portland, Oregon, the far-seeing Dr. Robert L. Swain presented a resolution, which was adopted, outlining a statistical survey and citing the necessity for a full understanding of the conditions under which Pharmacy is practiced in the various states as the soundest basis for legislation and pharmaceutical betterment.

The resolution was very explicit as to the types of information to be gathered and the central office of the ASSOCIATION undertook the job without realizing just what we had bargained for. We willingly admit, however, that the background of information gained as a result of this study has been of inestimable value to us in our work.

We have all heard of the three types of liars—of which the worst is the statistical liar. Statistical methods are simply a set of tools which are used to obtain,

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* Section on Education & Legislation, A. PH. A., Minneapolis meeting, 1938.

[1] Secretary, N. A. B. P., 130 N. Wells St., Chicago, Ill.

analyze and present a large mass of data. The measurements can be made as accurately as the mathematical formulas permit. The error comes in when statistics are used to prove something, a use never intended. The conclusions reached on the basis of the figures are only as good as the logic and common sense of the person formulating them. Hence interpretations often do not agree. In our N. A. B. P. survey published in 1936, we drew no conclusions—simply commented upon conditions in each state and the person reading the report is given the privilege of formulating his own conclusions.

One of our great surprises was the wealth of information available, particularly from the Census reports over a period of years, which Pharmacy seems to have more or less disregarded, particularly of a commercial or economic type.

To give an example: In the Census of Business—Retail Distribution, you will find the independent drug stores of the country classified as to volume of sales; also the chain and mail order outlets. Did you know, for example, that the largest of the independent groups is the class doing from $10,000 to $20,000 worth of business per year and it constitutes 32.6% of the total stores? Some one asked us recently "How many drug stores in the country do over $20,000 business annually?" We searched the census reports and found the answer: In 1935, 29.6% of the stores in the country were in this class. Only 3.8% of the independent stores were in the $50,000 or over classification but 64.7% of the chain and mail order outlets were in that class.

As boards of pharmacy, however, these commercial and economic questions are of interest to us only in the sense that a pharmacist must make money to remain in business and be able to render professional services when needed. So we carefully studied the per capita expenditure in various states, the number of stores on a population basis, the number of pharmacists and students in proportion to stores and population, etc. These commercial statistics, however, are of little value in judging the number of pharmacists needed. Legally anyone may sell proprietary remedies, cosmetics, cigars, fountain drinks, etc., which constitute a large portion of the total sales volume. Only 12.2% of this volume is prescription work, 34% is drugs, including patent and proprietary sales, and the balance of the items are not exclusively restricted to the drug store.

In the end, we found that no two states were exactly alike and that each needed a careful study of underlying conditions. Some states seem to have too many pharmacists and too many drug stores—others seem to have room for greater development. However, there seems to be a fundamental and constant adjustment of supply and demand which probably can be trusted as a better regulator than any device we may be able to set up. So long as our system of reciprocity functions smoothly, a redistribution of pharmacists can be worked out with little delay as changing economic conditions in the various states warrant.

The argument has been advanced that if there is an expansion in retail drug store sales back to say the 1929 level, there will be an acute shortage of registered pharmacists. This viewpoint cannot be logically accepted, in view of the fact that a considerable proportion of this increase is in items not restricted to the drug store. Prescription work is probably the most stable item. The number of physicians in proportion to population does not vary greatly, the annual cost of illness has been computed so that group clinics and even hospitals are able to quote annual rates at

so much per capita, and if we were to make a detailed study of the number of prescriptions compounded annually and other like professional services, we would probably find them equally stable. In fact, such a study should be undertaken by the various state associations.

Several estimates from reliable sources place the annual volume at 200,000,000 prescriptions, which is less than ten per drug store daily and less then six per pharmacist, although, of course, not evenly distributed. However, inasmuch as the pharmacists of the nation are constantly urging that the physicians write more prescriptions and various campaigns have been undertaken to bring this about, the number could probably be doubled without much difficulty other than perhaps a shifting of personnel in certain locations. The boards of pharmacy have no right to go beyond their legal prerogative and that is limited strictly to the professional duties for which a license is issued.

Last year, Dr. E. F. Kelly read a paper at this Section in which he estimated the needed replacements in personnel at from 3 to $3^1/_2\%$ of the total number of registered pharmacists, or approximately 3000 to 3500 new registrants annually. The N. A. B. P. studies show that close to this number have been registered each year for the past three years when the count was taken. Just to check up further, particularly after the discussions at last year's convention, we ran through the trend of registration as established for the eleven-year period 1925–1935, inclusive, and found that our final total was approximately 3300. It was necessary to make reasonable estimates for some of the states where no detailed data had been submitted.

The vital need of pharmacy, in our opinion, at the present time is to get a sufficient number of *adequately trained* pharmacists. Of these, there seems to be a shortage. We find this reflected in the contradictory reports from time to time. For example, we hear that the entire graduating class have positions months before the college term is over, and then on the other hand, we have reports from that same state of registered pharmacists unable to secure employment. Questioning often reveals that the latter class have had little or no college training, are too old, etc.

Also, there are many avenues of endeavor now open to the young man or woman receiving the four-year degree in pharmacy and it is not surprising to find some of them choosing lines of endeavor other than retail pharmacy. Again questioning reveals that the principal detriment so far as retail pharmacy is concerned is the long hours. Recently a young man who had deserted Pharmacy for football coaching asked why he should be expected to work for 40¢ per hour, when an unskilled laborer can earn that. Retail Pharmacy needs to keep a goodly number of these four-year graduates, particularly in view of the rapid progress being made in the field of new medicines. Such men have the basic scientific training to approach the physician in detailing for the pharmacist, and there is no reason why the individual pharmacist should not detail the physician as the manufacturer does. He is in a better position to do so, and it is the only way in which he can build up his prescription department. With efficient management and coöperation, hours can be cut without too great a loss in sales. Here, then, is a problem retail Pharmacy must consider and solve.

Now for a few figures to live up to the title of the paper: In June 1936, there were 8184 students enrolled in colleges of pharmacy; in June 1937, 8424 students

were in school; in the latest count June 1938, the number was 8190. In other words, the 3% increase of last year has again been wiped out. A contributing factor, however, has been the enforcement of the four-year course as the minimum in New York. While the enrollment totals for 1936 and 1938 are practically the same, there is an actual increase of approximately 150 students in other states because of a decrease to that extent in the New York figure.

A study of the student count by states and groups of states reveals a variety of trends. For example, we find that in *six* states Maryland, Massachusetts, New Jersey, New York, Oklahoma and Rhode Island enrollment has steadily decreased over the three-year period. However, all but one of these states had more students per store in college than the national average for 1936, so this may be a natural adjustment.

We find another group of *nine* states in which the enrollment has steadily increased during this period. These states are: Alabama, Connecticut, District of Columbia, Kansas, Kentucky, North Dakota, Ohio, Texas and Wisconsin. In Texas, the 1938 enrollment is 75% over that of 1936—but this is readily understandable to anyone in touch with conditions in that state.

There is another group of *eight* states, in which the June 1938 enrollment is above that of June 1936 but does not quite equal the higher figure established for 1937: Colorado, Minnesota, Missouri, Tennessee, Virginia, Washington, Georgia and Michigan.

In the final group of *nine* states, the 1938 enrollment is lower than that of either 1936 or 1937 but the decline has not been progressive: Illinois, Nebraska, Indiana, Iowa, Louisiana, Mississippi, Montana, Oregon and South Dakota.

Here is a point we want to emphasize: We brag that Pharmacy is almost universally on the four-year college basis and yet only about one-half of the 3000 pharmacists we register annually are graduates, if we compare the senior student count with the number of board registrants for the same year. This spread seems to be too wide—not all of the balance can be flunkers from previous years, or those just completing experience requirements. A considerable portion must still be quiz school products or assistant pharmacists and others coming in under special exemptions. Here, then, is the real problem—to fight and cut down on these exemption leaks so that an increase in college enrollment will be warranted.

The opportunities in Pharmacy, as in everything else, are limited. When we let poorly trained men in by the back door, we deny ourselves the better trained material that would be willing to come in by the front door—by meeting the degree requirement.

While the N. A. B. P. has opposed the use of publicity seeking to attract High School students into Pharmacy on the plea of a shortage of pharmacists, the Association realizes the necessity of eventually building up a larger student body so as to have say 3000 graduates available annually. To foster this, the central office sponsors a free vocational guidance service and sends out hundreds of envelopes of printed material to High School students, vocational guidance counselors, authors of vocational texts, etc. These valuable contacts should assist in attracting the right type of students from a long range point of view. The vocational guidance counselor wants facts not propaganda and for that reason statistics seem to be the most sought after form of information.

THE NEWLY ENACTED FOOD, DRUG AND COSMETIC ACT, AND ITS RELATION TO PHARMACEUTICAL LEGISLATION.*

BY ROBERT L. SWAIN.[1]

The enactment of this law must be regarded as one of the most important events in the public health field in recent years, and it is certain to exercise a profound influence throughout the entire field of pharmaceutical legislation. The state food and drugs acts, almost without exception, are copies of the Federal Law passed in 1906. It was the avowed purpose of these state laws to supplement and complement federal legislation and thus the closest uniformity was practiced with respect to the actual language of the acts.

Obviously, the recently enacted law has thrown this arrangement out of gear and will necessitate a revision of the food and drugs acts of the several states, if the same continuity is to be preserved. This was, of course, to be expected and some thought has already been given to making the state acts conform to the new pattern.

Little thought, however, has been given to what the Federal Food, Drug and Cosmetic Act may mean to pharmacy laws, but it is my feeling that the new law affords an unusual opportunity for extending the authority of pharmacy laws and throws new light upon the whole effort now being made to modernize pharmaceutical legislation.

The Federal Food, Drug and Cosmetic Act clearly outlines the field in which it is to operate by comprehensive definitions of the subject matter to which it shall apply, and this fact alone should be seized upon as an essential factor to be considered in the revision of pharmacy laws. It is interesting to note that while pharmacy laws have to do almost exclusively with drugs, only a small minority of the state pharmacy laws attempt any definition of this term. In other words, the pharmacy laws proceed to discuss the rights and privileges of pharmacists with respect to drugs, the education which pharmacists must possess in order to deal intelligently and competently with drugs, and the prohibitions against others than pharmacists selling drugs, and yet, nowhere in the laws is there to be found any legislative pronouncement as to what the term "drugs" includes, and even in those few pharmacy laws in which an attempt is made to define the word "drugs," it will be found that the passage of the Federal Food, Drug and Cosmetic Act has rendered the definitions obsolete.

In order that we may truly appreciate the significance of the change which the new legislation has brought about, it will be helpful if we quote the definition of the term "drug" from the act originally passed in 1906, the definition as it now appears in the Federal Food, Drug and Cosmetic Act, and contrast this latter definition with the definitions of the term "drugs" as they appear in the pharmacy laws of the states given below.

FOOD AND DRUGS ACT OF 1906.

The term "drug," as used in this act, shall include all medicines and preparations recognized in the United States Pharmacopœia or National Formulary for

* Presented before the Section on Education and Legislation, A. PH. A., Minneapolis, meeting, 1938.

[1] Secretary, Maryland State Board of Pharmacy.

internal or external use, and any substance, or mixture of substances, intended to be used for the cure, mitigation or prevention of disease, of either man or other animals.

FEDERAL FOOD, DRUG AND COSMETIC ACT.

The term "drug" means (1) articles recognized in the official United States Pharmacopœia, official Homeopathic Pharmacopœia of the United States or official National Formulary, or any supplement to any of them; and (2) articles intended for use in the diagnosis, cure, mitigation, treatment or prevention of disease in man or animals; and (3) articles (other than food) intended to affect the structure or any function of the body of man or animals; and (4) articles intended for use as a component of any article specified in clause (1), (2) or (3); but does not include devices or their components, parts or accessories.

At this point it might be well to point out that the new definition recognizes the Homeopathic Pharmacopœia of the United States, as well as all supplements issued to the United States Pharmacopœia, National Formulary or Homeopathic Pharmacopœia, and brings within the classification of drugs, many new articles not heretofore specifically so regarded, such as articles used in the diagnosis and treatment of disease. Also, many articles, particularly those affecting body function and structure, such as "obesity cures," which heretofore were not regarded as drug products, in that they were not used in the cure, mitigation or prevention of disease, are now brought within this classification.

A study of the new definition in its entirety will impress one with the fact that the term "drug" has taken on a vastly expanded meaning and to the same degree has become of the greatest significance to the whole body of pharmaceutical legislation.

Let us now note the contrast between the state pharmacy laws and the Federal Food, Drug and Cosmetic Act in respect to the meaning of the words "drug" or "drugs."

Alabama.—"Drug" or "Drugs," where not otherwise limited, means any substance or substances used as medicines or in the preparation of medicines.

"Medicine" or "Medicines," where not otherwise limited, means a drug, drugs, chemicals, compounds or preparations thereof, in suitable forms for use as curative or remedial substances, either internally or externally by man or for animal.

"Chemical" or "Chemicals," where not otherwise designated or limited, means definite chemical compounds or the chemical materials of medicines.

Arizona.—The term "drugs," where not otherwise limited, means any substance used as a medicine or in the preparation of medicines.

The term "medicines," where not otherwise limited, means drugs or chemicals, or compounds, or preparations thereof, in suitable form for use as a curative or remedial substance intended to be used either internally or externally for man.

The term "chemicals," where not otherwise limited, means definite chemical compounds, or chemical compounds or materials or medicines.

Arkansas.—The term "drug," as used in this Act shall include all medicines and preparations recognized in the United States Pharmacopœia or the National

Formulary for substances intended to be used for the cure, mitigation or prevention of disease of either man or other animal.

"Medicine," when not otherwise limited, means a drug or preparation of drugs, in suitable form for use as a curative or remedial substance.

Iowa.—"Drugs and medicines" shall include all medicinal substances and preparations for internal or external use recognized in the United States Pharmacopœia or National Formulary, and any substance or mixture of substances intended to be used for the cure, mitigation or prevention of disease of either man or animals.

Minnesota.—The term "drug" shall mean all medicinal substances and preparations recognized by the United States Pharmacopœia and National Formulary or any revision thereof, and all substances and preparations intended for external and internal use in the cure, mitigation, treatment or prevention of disease in man and animals, and all substances and preparations, other than food, intended to affect the structure or any function of the body of man or animals.

The term "medicine" shall mean any remedial agent that has the property of curing, preventing, treating or mitigating diseases, or that is used for that purpose.

"Chemical" means all medicinal or industrial substances, whether simple or compound or obtained through the process of the science and art of chemistry, whether of organic or inorganic origin.

Nebraska.—For the purposes of this article "drugs and medicines" shall include all poisons, dangerous or deleterious substances and preparations for external or internal use recognized in the United States Pharmacopœia or National Formulary which are intended for the correction, mitigation or prevention of diseases of either man or animals, or any other poisonous, dangerous or deleterious substances and preparations intended for a similar purpose, except patent or proprietary medicines.

New Hampshire.—"Drugs," when not otherwise limited, means all substances used as medicines or in the preparation of medicines.

"Medicine," when not otherwise limited, means a drug or preparation of drugs in suitable form for use as a curative or remedial substance.

New York.—"Drugs," where not otherwise limited, means all substances used as medicines or in the preparation of medicines. "Crude Drugs," means drugs that have not been changed by manufacture except desiccation or comminution.

"Medicines," where not otherwise limited, means a drug or preparation of drugs in suitable form for use as a curative or remedial substance.

Oregon.—"Drug" or "Drugs," where not otherwise limited, means any substance or substances used as medicines or in the preparation of medicines.

"Medicine" or "Medicines" where not otherwise limited, means a drug, drugs, chemicals, compounds or preparations thereof, in suitable form for use as a curative or remedial substance, either internally or externally by man or for animal.

"Chemical" or "Chemicals," where not otherwise designated or limited, means definite chemical compounds or the chemical materials of medicines.

Pennsylvania.—The term "drug," as used in this act, shall include all medicines and preparations recognized in the latest revision of the Pharmacopœia of the United States, the latest edition of the National Formulary or the American Homeopathic Pharmacopœia, or any supplement to any of them official at the time of investigation, for the internal or external use and any substance or mixture of substances, intended to be used for the cure, mitigation or prevention of disease of either man or animals.

Rhode Island.—The terms "drugs," "medicines" and "poisons," as used in this chapter, shall mean and include all drugs and preparations sold under or by a name recognized in the United States Pharmacopœia or National Formulary, and of the standards of strength, quality or purity as determined by the test, if any, laid down in the United States Pharmacopœia or National Formulary.

South Dakota.—"Drugs," where not otherwise limited, means all substances used as medicines or in the preparation of medicines and such material as may be used in the treatment of disease.

"Medicines," where not otherwise limited, means drugs or chemicals, or preparations thereof, in suitable form for the prevention, relief or cure of diseases, when used either internally or externally by man or for animal.

"Chemicals," where not otherwise limited, means the chemical materials or (of) medicine.

Virginia.—The word "drug," as used in this chapter, shall include all medicines and preparations recognized in the United States Pharmacopœia or National Formulary for internal or external use, and any substance or mixture of substances intended to be used for the cure, mitigation or prevention of disease of either man or other animals.

Simply in passing, it is interesting to note that under the Nebraska definition, all articles intended for the correction of disease are classed as drugs, the same thing being true of poisonous, dangerous or deleterious substances and preparations intended for similar purposes. Most interesting, too, is the provision that patent and proprietary medicines are not drugs under the pharmacy law of that state.

A study of the above definitions will be found interesting and will afford much food for thought, but even a casual reading is sufficient to show that they are not as comprehensive and not as broad as the definition in the Federal Food, Drug and Cosmetic Act.

It must be apparent by this time that one of the major defects in our pharmacy laws is that of basic definitions, and it must be apparent, too, that the term "drugs" should have the same meaning in pharmacy laws as that ascribed to it in other related legislation.

There would seem to be no logical basis for defining the term "drug" one way in federal or state food and drugs acts, and another way in pharmacy laws, because there is a direct relation between pharmacy laws and food and drugs acts. The food and drugs acts set up standards for drugs and medicines, adopt prohibitions against their misbranding and adulteration, and prescribe penalties for violation. The pharmacy laws deal with the educational qualifications of those who shall prepare drugs and medicines, who may dispense them, and the conditions surrounding the compounding and dispensing of physicians' prescriptions for drugs and medicines.

There would seem every reason why the basic definition of drugs should be the same in the pharmacy laws and in the food and drugs acts. This point is emphasized because in the past, there has been no disposition to adopt uniform definitions, even in the food and drugs act and the pharmacy law of the same state. This, no doubt, has contributed toward a lack of coöperation between enforcement agencies concerned with the administration of the food and drugs acts and those charged with the administration and enforcement of pharmacy laws.

It is my judgment that an attempt should be made to bring about uniformity so that the pharmacy laws may be broad enough and comprehensive enough to encompass that field of drugs and medicines which is covered by the food and drugs acts. I believe this will result in greatly expanding the scope and authority of pharmacy laws, will have a tendency to more sensibly limit the distribution of drugs and medicines to pharmacists, and will afford the public a much greater degree of protection in this highly important matter. At any rate, it opens up a new field of study and one which should receive the very closest consideration of all interested in a modernization of pharmacy laws in a real and modern sense.

MUST ONE KEEP OPEN AT NIGHT TO COMPOUND PRESCRIPTIONS?*

BY FRANK A. DELGADO.[1]

An invitation to spend the week-end with friends at their summer cottage near East Hampton, L. I., was gladly accepted as it presented an opportunity to escape the heat wave that had been raging in New York. That evening some neighbors called, and introductions followed. My host said "Meet Mr. Doe. He is a pharmacist but like yourself has not actively practiced it for many years." I asked Mr. Doe what was his occupation at present, and what led him to give up the drug business. He informed me that he was now in the hardware business and I was to learn later that Fortune had smiled upon him, and that he not only possessed a splendid business which netted him an excellent income, but that furthermore he was getting the most out of life. He had a fine home, two new automobiles and some income property. He and Mrs. Doe visited New York City frequently to attend the theater and otherwise amuse themselves. He had two splendid sons of whom he had reason to be proud. His business while most profitable did not prevent him from enjoying the society of his family, and indulging in fishing and outdoor sports of which he was very fond. He decided to quit the drug business, he said, when one night after one A.M. he was awakened by a customer who asked would he compound a prescription. He slid into some clothes and still half-awake accompanied the supposedly sick man to the drug store. Switching on a light he read the prescription, and to his anger and amazement found that it was of the tonic variety, and furthermore bore a date that showed the patient had been carrying it around in his pocket for two or three days. It was precisely at this moment that Mr. Doe decided to seek his livelihood in some other field.

The incident just related may be exceptional; however, I venture to say that a study of the prescriptions dispensed after six P.M. would show that a substantial

*Presented before the Section on Pharmaceutical Economics, A. PH. A., Minneapolis meeting, 1938.

[1] 34-24—82nd St., Jackson Hts., New York City.

number could have been held until the next day. It is not infrequent that a physician leaves a prescription with the patient in the morning or afternoon, who waits until evening when some member of the family will visit the drug store to have it compounded. They know only too well that they will find the pharmacist on the job. It is unfortunate that the professional duties of the pharmacist are made to bear the brunt of the blame for the ridiculously long hours that pharmacists work. Anyone familiar with the facts should know that the long hours prevailing in the drug store are the result of commercial activities, since transactions that take place at night are much more apt to be at the cigar counter or soda fountain than behind the prescription counter. This is brought out in "The Professional Pharmacy," the National Drug Store Survey report, published by the AMERICAN PHARMACEUTICAL ASSOCIATION. This pictures the flow of the prescription business in three professional pharmacies, according to various periods of the day.

In Stores A and C the period from 3:00 to 6:00 P.M. had the largest number of prescriptions, but the two preceding periods from 11:00 A.M. to 1:00 P.M. and from 1:00 to 3:00 P.M. really had the heaviest volume inasmuch as each of these periods is only two hours in length as compared with the three hours between 3:00 and 6:00 P.M. In Store D the two periods running from 11:00 A.M. to 3:00 P.M. were clearly outstanding. In Stores A and C, the opening period from 8:00 to 11:00 A.M. and the closing period from 6:00 to 9:00 to 10:00 P.M., both being at least three-hour periods, clearly had the lightest volume of prescription business. In Store D the closing period, from 6:00 to 10:00 P.M. had the lightest volume, but the opening period in the morning had quite heavy volume.

Thus it can be said that the professional pharmacy, generally speaking, will have its heaviest volume of prescription practice from 11:00 A.M. to 3:00 P.M., and its lightest volume in the evening after 6 o'clock, and during its opening period in the morning. Store location may vary the time of day in which business is heaviest, but as professional pharmacies generally have a central location, most of them will probably encounter the same conditions. In Stores C and D the Sunday hours were only half as long as for the other days of the week, but the prescription business amounted to less than one-third of the usual daily volume. Store A was open from 9:00 A.M. to 4:00 P.M., although practically the entire Sunday prescription work is done within a three-hour period, from 10:00 A.M. to 1:00 P.M. It will be seen that it is not so essential for the professional pharmacy to keep long hours and that it is not the prescriptions which are responsible for the long business day of the commercial type pharmacy. Younger pharmacists who feel a repugnance to the long fourteen, sixteen and eighteen-hour days of the commercial type pharmacy, will be drawn to the professional pharmacy, where the hours are generally shorter, and in many cases could be made even shorter by closing after 6:00 P.M. and on Sundays when in many cases, it would probably be more profitable to close the establishment. It is not unreasonable to suppose that shorter hours would attract a desirable type of young men.

The matter of opening and closing hours depends largely on the location and to some extent on the inclination of the owner of the pharmacy. This is also true relative to Sunday hours; the greater number of pharmacies are open on Sundays and in some the receipts are larger than on other days. Many stores close for part of Sunday, some close all day. The examples given may be of interest. One

pharmacist in a large city adopted Sunday closing, advertising the venture in the daily papers prior to making his decision effective. The results were so satisfactory that this pharmacist has continued the practice started in 1919. He refers to Sunday leaks as amounting to quite an item, perhaps more than offsetting the profits. Another pharmacist continued the practice of Sunday closing, because his business increased as a result; a number of patrons gave this among their reasons for patronizing this pharmacy.

Of the thirty-three stores dealt with in the study, the majority opened at 8:00 A.M. and closed at 10:00 P.M. on week-days, while the average Sunday hours are from 9:00 to 9:00 P.M. Two of the stores do not open on Sunday. As for the Sunday prescription business, one store reported it heavy, three good, five only fair and twenty-four (or 73 per cent) poor. Fresh evidence that long hours and compounding prescriptions do not necessarily go hand-in-hand is furnished by the new prescription department recently inaugurated by R. H. Macy & Co. of New York, which has announced that it will abide by the regular store hours which are from 9:30 A.M. to 5:30 P.M. The store is closed on Saturdays during the summer and on Sundays the year round. Employee pharmacists are naturally attracted by employment in prescription departments of the type mentioned above. If we must work fifteen or sixteen hours a day, let us be honest and admit that we do so purely for commercial gain and not because of our professional responsibilities.

THE PLACE OF THE PROFESSIONAL DISPLAY IN A PHARMACY.*

BY M. MEDFORD COOPER.[1]

What is meant by the phrase "professional display?" It means one which calls to the attention of the public the need for medical care, explains a pharmaceutical process, or in some other way suggests that the pharmacist, apart from merchandising, is professionally trained. Some of these displays may be strictly professional, others may indirectly advertise ethical products.

About two years ago, I became particularly interested in the average pharmacist's attitude toward displays, especially toward professional ones. I made it a point to question pharmacists in different sections of the state whenever the opportunity offered. The average response was something like this, "A professional display may be all right during pharmacy week because others do it, but people aren't interested in that sort of thing. All they want to know is where they can buy things the cheapest. They know drug stores fill prescriptions without being told about it."

I didn't agree with them. I believed that the public would be interested in professional displays and that such displays should be of definite value in dollars and cents.

In our college I am charged, among other things, with the responsibility of store practice in our model pharmacy. With this as an opportunity, I started my students building professional displays, trying them in the windows of the model

* Presented before the Section on Commercial Interests, A. PH. A., New York meeting, 1937.

[1] Instructor in Economics, Albany College of Pharmacy, Albany, N. Y.

store and then taking them out to windows of stores around the capital district. The response has been gratifying.

We have placed such displays in different types of stores. In every instance the pharmacist has told me that more people have examined our display than any they have had in the window for a long time. In many cases people have gone into the store to ask questions about it. Some of these people have been regular customers of the store. Other store owners, after observing the attention the public has given to these windows, have telephoned me to find out whether they, too, could have one. A regular customer of one store said to the pharmacist, "I didn't know you were interested in that side of pharmacy. I thought you just wanted to sell patent medicines and other things." In another instance a neighborhood doctor was attracted by the display, stopped in to talk with the pharmacist, and, as a result, started sending his patients there.

These experiences, even though limited, prove to me that professional display has a vital place in the store program, a place which most pharmacists are ignoring.

I do not wish to minimize displays really intended to sell merchandise, but I do condemn those that give a prospective customer the idea that a drug store is merely a place in which he may buy something on Sunday which he forgot to get at some other store during the week. The prestige of the profession of pharmacy has suffered greatly in the minds of the public because the multitude of stores resemble anything but a drug store. However, the public will hold pharmacy in a higher respect, and, in the long run, supply as large or larger profits to the pharmacist who will follow a consistent program of professional displays.

Much has been written recently suggesting displays, letters to physicians, and open prescription departments as a means of increasing the prescription practice. This is surely a worthy objective. Personally, I am of the opinion that an increase in the sale of drugs other than those prescribed, is of equal or greater importance than the goal which has received so much attention.

Constant emphasis upon the need for preservation of health through professional displays cannot help but increase the sale of health items. For example, the average person probably uses a toothbrush three times as long as he should. It isn't because he hates to spend the thirty-nine or fifty cents, but because he doesn't realize that a new one would clean his teeth better. When he cuts his finger he thinks, "That's nothing," largely because he has no first-aid dressing handy. When his eyes are tired after a dusty drive he thinks, "Oh, well, they will feel better in the morning." He doesn't go to his medicine cabinet and use an eye wash, because no pharmacist has sold him on the idea of the greater comfort he might secure.

It is true that drug stores everywhere sell toothbrushes, band-aids and eye washes, but, to a large degree, they are sold on a price basis, along with a lot of other items. The customer upon walking into the store is confronted with an array of articles, each of which carries a price. The customer is price conscious rather than health conscious.

I do not pretend to claim that price display should be avoided entirely, but I do believe that the average pharmacist should show a professional display frequently. These are more valuable than the cardboard displays of products which may be purchased anywhere, or, at least, in any drug store. Then he should follow

it up inside the store with a portion of his space devoted to the display of drugs on the basis of health needs and preservation.

A store carrying out such a program is, eliminating legal definitions, rightfully entitled to call itself a "pharmacy." Others are better described merely as "drug stores," with emphasis on the "store."

SOME USES FOR COLOR IN THE DRUG STORE.*

BY GEORGE F. ARCHAMBAULT.[1]

The pharmacist's own use of color in the average store has been, up to the present, mostly confined to window and show-case displays. It is true that manufacturer's lithographs and the myriads of patent and proprietary medicines have created kaleidoscopic views upon our drug store shelves, but the truth still remains—more color could be used. The purpose of this paper is to point out some salient facts concerning color, both from the physical and psychological angle, and methods whereby color may be utilized to increase sales volume and good-will, at a trifling expense.

Color still remains one of the strongest optic attention-getting factors. Before many commodities are released to the public, they are "sales tested" in several different colored combination packages and dress, to ascertain exactly which combination of colors will produce the greatest sales appeal. Many brands of cotton are now packaged in blue with a blue inner wrapper since white cotton against the blue background appears still whiter. Comet rice packages are lined with blue at an extra cost of thousands of dollars annually. The increased sales, however, prove well the point that color is an invaluable selling aid.

Before attempting to give any actual applications of "color selling" several key facts that must be observed in producing proper color harmonies are here pointed out.

1. Materials react differently to light on account of their "surface quality" or texture. This phenomena is called "specular reflection" or "mirror action," and is due to the fact that some materials are flat and others are deep piled, some are dull and others shiny. These physical characteristics cause materials to catch or reflect light rays differently. Velvets, for example, contain thousands of little pockets which trap the light and prevent it from being reflected. For this reason, two different textured fabrics may appear to have different shades or tints when in reality they have been dipped in the same dye.

2. Electric and other artificial lights by comparison with daylight usually contain considerably more yellow or orange and less blue rays, and under such illumination blue objects have a tendency to appear green. Other colors are also affected. Therefore two colors which harmonize in daylight when viewed under artificial light may conflict. Test your color combination before using.

3. In building a monochrome harmony (several colors of the same hue) con-

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* Presented before the Section on Commercial Interests, A. PH. A., New York meeting, 1937.

[1] Instructor, Department of Business Administration, Massachusetts College of Pharmacy, Boston, Mass.

siderable care must be exercised in picking the proper shades or tints lest one appear to be faded.

4. Colors have a physiological influence. Generally speaking the colors which are at the red (orange, yellow) end of the spectrum are warm, active, stimulating, and sometimes, if overdone, irritating, while the colors at the purple (blue, green) end of the spectrum are cold, passive, quieting, and sometimes, when overdone, depressing.

Red increases the activities in the nervous system, while blue inhibits. Changes in the heart beat and respiration are caused by various colors.

5. Each color is capable of evoking definite mental impressions, referred to as the color's "feeling tone," due to the psychological effect created by the color through association of ideas. A color may therefore have either a pleasant or unpleasant feeling tone or both. The following list is not original with the author, but is included here because it covers the topic quite thoroughly, and will greatly aid pharmacists in selecting proper colors for feeling tone in selling.

"FEELING TONE" OR COLOR LANGUAGE.

Positive Feeling.	Color.	Negative Feeling.
Purity	White	Pallor
Innocence		Winter
Light		Blankness
Joy		Weakness
		Bleakness
		Paleness
	Black (opposite to white)	Sadness
		Contamination
Sunlight	Yellow	Treason
Metal gold		Cowardice
Happiness		Deceit
Cheerfulness		
Masculinity	Blue	Melancholy
Truth		
Coolness		
Reserve		
Honesty		
Adventure	Red	Cruelty
Femininity		Anger
Warmth		Danger
Fire		Ire
Passion		Sin
Vitality		
Health		
Royalty	Purple	Mourning
Luxury		Death
Dignity		Age
Wealth		
Reverence		
Religion		

6. In displaying men's goods, the colors red; second, green; third, orange, are the most effective, providing they harmonize with the color of the item being

displayed. Colors at the blue end of the spectrum are said to have less sales appeal to the average man.

7. Cellophane, glassine and like materials increase the sales ability of an item because they reflect light, creating a brightness and newness that customers attribute to the products wrapped in them. The pharmacist should use this truth often and generously.

8. By actual tests* under certain artificial lights, the following colors have been found to have the greatest sales appeal.

Product.	Color.	Nature of Color.
Perfumes	Yellow and purple	Weak
Soaps	Yellow and green	Saturated
Candy	Yellow and red	Saturated
Summer beverages	Yellow and green	Saturated

* Taken from tests conducted by N. Collins for his thesis at Columbia, 1924.

9. Where manufacturers' lithographs are to be used in a window display or counter unit, a handy general rule in selecting color harmonies, is that a pleasing color combination results from taking as the main background color either the color most prevalent in the lithograph or the one least prevalent. The first creates a blended harmony while the second makes for sharp contrast.

10. The five (5) most legible combinations of colored letters on colored backgrounds arranged in order of their legibility are:

Letter Color.		Background Color.
Black	on	Yellow
Green	on	White
Red	on	White
Blue	on	White
White	on	Blue

COLOR AND COSMETIC SALES.

Selling with color aids has, to the present time, been confined to the use of jewelers, but even here it has not been developed much beyond the basic stages. The sales price of the majority of novelty and luxury items is based upon the value given by the purchaser rather than the true value of the item. The visual appearance, that is, the dress and the manner in which the item is presented in the selling process, are important determinants of the value and selling price in the mind of the customer. Jewelers, in handling a stone or ring, regardless of its true value, never display the article in a mass of others, or hand it to the customer with a short sales talk. Such items are handled individually and with care, as though of great value. They are gently placed on fabrics (black or purple) and the fine features pointed out. The druggist can develop the same technique of selling and even carry the idea further by matching the colors of the item being sold with one of the several available "Selling Fabrics." Because the Cosmetic Department of a drug store contains the more frequently called for luxury and novelty items, detailed illustrations shall be taken as examples. Lipsticks and compacts usually come in two dominant colors: gold and silver. In selling a compact, gold in color, a selling fabric of approximately fifteen by eight inches may be used, preferably of white satin cloth. Besides matching the case, the white satin makes an excellent

background when the compact is opened. The lipstick likewise may be placed upon the "Selling Fabric" while the merits of the product are being pointed out. After the talk, the item is gently pushed, satin and all, toward the customer. It invites inspection of a "valuable item."

If silver should be the main color in the cosmetic container, the counter cloth may be of dark blue velvet. Other colors are of course acceptable if matched to the container and contents. A red color assumes a brillance on white or pale green and loses intensity on red or brown backgrounds. Other colors also intensify their hue on contrasting colors and appear dull on like colored backgrounds. The druggist who knows this fact, and has a selection of counter cloths, should never get complaints against color once he knows the customer's need.

COLOR IN THE PRESCRIPTION DEPARTMENT.

Color in the Prescription Department is not as far fetched an idea as it might at first appear. Every pharmacist should wish to emphasize the cleanliness and the quality of his establishment and prescriptions. Again color can be used effectively. Packaging pills and capsules in boxes lined with light blue paper will accentuate their whiteness and cleanliness. The same is true for powders folded in white papers. A layer of pale blue cotton in a white lined box makes pills and capsules easy and pleasant to take. Other colors may also be used.

OTHER USES FOR COLOR.

If the druggist manufactures his own preparations the proper choice of coloring agents becomes very important. Blue, or milk-white mouth washes are never popular, no doubt due to the "feeling tone" which suggests "unfitness for internal use." The best selling mouth washes are on the red end of the spectrum. Two of the fastest selling mouth rinses of the day bear out this point. One, a red, is suggestive of health and vitality; and the other, an amber, is likewise suggestive of health, sunlight and cleanliness.

Another possibility is the use of colored caps for prescription bottles. A white cap is never objectionable and caps matching in color the liquids dispensed create favorable impressions upon patients.

The receptive mood of the customer is markedly affected by color in more distant objects, or by color as an abstract phenomenon. For instance, it has been said that green helps sell summer beverages. Doesn't that suggest green light on the fountain backbar, green trimmings on the uniforms of the fountain help? Colored light and color may also be used in the individual show-case to advantage, also in the stationery of the pharmacy, in the wrapping paper, and in the twine or tape. A pleasant harmony will create a store color personality, so to speak, which will automatically bring the particular pharmacy to mind whenever the color or combination of colors is seen in the community.

PAST AND PRESENT OBSERVATIONS OF DRUG STORES.*

BY MATHIAS NOLL.[1]

After forty years in the drug business, my great regret is that the drug store, the kind in which I learned to be a pharmacist, has lost its identity and that the

* Presented before the Historical Section, A. PH. A., Minneapolis meeting, 1938.

[1] Retired pharmacist, Atchison, Kansas.

character it once had is no longer recognizable. It is impossible for me to reconcile the fact that Pharmacy as a profession, which I spent so much time and money to learn, and years of experience as an active druggist to perfect, could have completely changed complexion as far as the public is concerned.

We thought we had everything when the Pharmacy and Registration Laws passed; before that any blacksmith with a few thousand dollars could buy up a drug store and call himself a druggist.

No other type of store could compete with the old-time drug store in human interest. A grocery store had a stomach, but the good old drug store had a heart in it. In sickness, health, pleasure, woe or leisure, the drug store had no rival. It seemed there was something in the sign of the Apothecary that made people want to go into a drug store whether they wished to buy or not. There they found the touch they could get nowhere else; to spend a few waiting minutes was a privilege not so valued in any other place. What appealed to them most, we druggists could only imagine from the pleased expression on their faces. We didn't know but that they came in because of the aroma of good cigars in the case, the odor from the sweet-scented soaps and perfumes, the gold fish, the long rows of pretty bottles of uniform size (containing medicine, of course), all lettered in gilt, which were kept on the shelves. And let me not forget that first drug store, where I washed bottles packed in straw, trimmed the coal-oil lamps, dusted the old sponge basket sitting in the center of the floor and cleaned the colored show globes in the window which were the chief decorations.

There is a tinge of sadness in the thought, and I can't quite realize it to be true, that the place I once owned and operated for forty years, known to all men as a drug store, is no longer in existence. I have a hard time trying to explain to my young grandchildren the difference in the drug store I sold less than twenty years ago, and the one they see to-day. I can imagine them telling me that they don't see anybody at the store doing things in the way I said I used to do them, and they might keep the idea to themselves, that Grandpa couldn't have been much of a druggist anyway.

ELISHA DEBUTTS, PHYSICIAN, CHEMIST, TEACHER, DEAN AND DELEGATE TO THE 1820 UNITED STATES PHARMACOPŒIAL CONVENTION.*

BY LYMAN F. KEBLER.[1]

During my studies of the activities of that versatile super-man, Dr. Samuel L. Mitchill (1) in stimulating uniformity in the manufacture of medicines, in aiding unification in the writing of prescriptions and establishing drug standards, the activities of Dr. DeButts came to the fore. Little is of record of his work in the above fields. He was one of the five physician-chemists, who took a prominent part in supporting the first United States Pharmacopœial Convention and the results issuing therefrom. The five physician-chemists were Lyman Spalding, Samuel L. Mitchill, Elisha DeButts, Wm. MacNevan and Joseph Parrish. Dr. DeButts took a continued active part in the work.

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* Presented before the Historical Section, A. PH. A., Minneapolis meeting, 1938.

[1] Former Chief of the Drug Division, Bureau of Chemistry, U. S. Department of Agriculture.

Elisha DeButts (1773–1831), of Irish extraction (2), came to this country with his parents, age about thirteen, about the time of the Twelfth Continental Congress. He was sent to live with his uncle, Dr. Samuel DeButts, in Alexandria, Virginia, where he attended school and grew into manhood. His medical studies were probably begun with his uncle and continued in the University of Pennsylvania, where he received his medical degree in 1805. Elisha, like Samuel Mitchill, had the advantage of being reared in a medical atmosphere. While engaged in his medical studies he came under the benign influence of the ingenious James Woodhouse, dean and professor of chemistry in the Medical School of the University of Pennsylvania. He also probably came into personal contact with Benjamin Smith Barton, John R. Coxe, Adam Seybert, Benjamin Rush, Robert Hare, Samuel Cooper, Caspar Wistar and other prominent scientists, who were either domiciled or studied in Philadelphia at the time, the scientific center and the largest city in the United States. The Philadelphia Chemical Society was then in a flourishing condition and brought many distinguished scientists to its meetings; certainly an inspirational environment for a young man in which to acquire an education. Furthermore Dr. Barton was then collecting data for a future American Pharmacopœia. In 1804, he discussed drugs (3), before the Philadelphia Medical Society, which he believed should be included in such a pharmacopœia, when it is developed.

ELISHA DEBUTTS.

After acquiring his medical degree the doctor practiced medicine on the Potomac, in Alexandria and Washington (2), for several years and later made Baltimore his home. In 1809 he was appointed to the chair of Chemistry in the Maryland College of Medicine, rendered vacant by the death of John Shaw, the first professor of Chemistry in the college. A few words about Professor Shaw would seem to be appropriate. John Shaw (1778–1809), a Bachelor of Arts alumnus of St. John's College of Annapolis, one of the founders of the Maryland College of Medicine, studied medicine in Philadelphia and Edinburgh, accepted a medical appointment in the United States Navy, later practiced medicine as a partner of his preceptor in Annapolis, but never received a degree in Medicine. In 1807 he publicly offered his services to the people of Baltimore, began a series of private lectures in Chemistry, and in November or December was appointed to the chair of Chemistry. He died at sea while in search of health, January 10, 1809.

Acting on a memorial of the president and the professors of the Medical

College, the General Assembly of Maryland in 1812 established the University of Maryland (4). Dr. DeButts because of his professorship is credited as one of the founders of the University. His title then was Professor of Chemistry and Mineralogy. He served as dean of the Medical College in 1816 and again from 1822–1824. To this office he brought great honor. During his deanship he had the privilege of seeing the University confer the honorary degree of L.L.D. on Major General Marquis de Lafayette, while the latter was visiting the United States. The faculty chose Dr. DeButts in 1812 as a delegate of the Middle District to the National Pharmacopœial Convention. He met with the other four delegates of the Middle District in Philadelphia, June 1, 1819. These five delegates remained in session for five days and evenings, preparing a rough draft of a proposed Pharmacopœia. The rough draft was sent to the Pharmacopœial Convention in Washington. The five delegates were the five physician-chemists alluded to above.

The general write-ups of the first National Pharmacopœial Convention give one the impression that the work was accomplished in a day or so, but the contrary is true. Six delegates met in Washington, Saturday, January 1, 1820, spent the day on the material submitted and adjourned late in the day to meet the following Monday. On Monday five more delegates reported for duty. The delegates spent the entire week, discussing, revising and comparing notes. During these meetings the delegates certainly had an opportunity to ascertain who of them was best qualified and in position to carry the work to completion, after the convention adjourned. Dr. DeButts was named on the committee of publication, appointed before the delegates adjourned. Three of the six members of the committee were physician-chemists.

The duties of the committee on publication included a revision of the work, preparing it for the printer and providing for the publication of the Pharmacopœia, the first edition of which was copyrighted December 15, 1820. This is the date of its publication as usually given. The committee met in New York, New Haven, Hartford and Boston. To what extent Dr. DeButts attended these meetings is not of record but there is immediate evidence that he was a member of the editing committee and corrected portions of the page proof of the first United States Pharmacopœia. These are in the possession of Editor E. G. Eberle, through whose kindness they have been reproduced and made available. The authenticity of the page proof is certified to by a letter in the handwriting of Dr. Spalding. The annotations show that Dr. DeButts was required to give immediate attention to the chemical features involved. On page nineteen, in longhand, appears the following: "*Saml. L. Mitchill. Scribe.*" which shows that Dr. Mitchill took an active part in correcting the page proof.

The eminent Dr. Edgar F. Smith, chemist, historian and provost of the University of Pennsylvania, in his "Dedicatory Address," dedicating the Chemistry Building of the University of Maryland in November 26, 1927, in reference to Dr. DeButts said: (5) "This science (Chemistry) and this University (Maryland) had great lustre shed upon them by Elisha DeButts through his eloquence, his skill in manipulation and his deep knowledge of the science. It has been said 'that as a teacher of chemistry he was perhaps unequalled'—certainly unexcelled—."

The chromium industry of Baltimore had its beginning during the time of Dr. DeButts and it is believed by some that he was an active participant in its develop-

ment but so far nothing of an authentic character has been located on the subject.

From my study of the life, work and accomplishments of Dr. Elisha DeButts I feel justified in calling him the first prominent physician-chemist of the State of Maryland.

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(1) Kebler, Lyman F., "The President of the First Convention Called to Formulate the United States Pharmacopœia," JOUR. A. PH. A., 26, 908 (1937).

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(3) Collection for an Essay toward a Materia Medica for the United States, published privately by the author.

(4) Cordell, Eugene F., "Historical Sketch University of Maryland," 24 (1891).

(5) Private communication from the Edgar F. Smith Memorial Collection of the University of Pennsylvania.

A BRIEF HISTORY OF COMMERCIAL MEDICINAL PLANT CULTURE IN THE UNITED STATES.

At a recent meeting of the City of Washington Branch, A. PH. A., A. F. Sievers, Senior Biochemist, Division of Drugs and Related Plants, Bureau of Plant Industry, Department of Agriculture, read a paper under the above title.

The following is a summary of the paper.

The possibilities of growing medicinal plants for the crude drug market have interested persons in all walks of life and in all parts of the country. It seems to have a special appeal to almost all classes. Few persons are really qualified to undertake such a project because it requires special knowledge of plant culture and the evaluation of the crop in many cases requires technical skill and equipment. Moreover the economic aspects are so frequently not thoroughly understood or given insufficient consideration.

A review of the attempts at commercial drug plant culture in the United States and a study of the factors and circumstances that accounted for their success or failure provides a fairly clear picture of the question as a whole. In fact the prospects of such an industry in the future may well be judged from the records of attempts in the past. Successful competition with foreign sources of supply appears no more likely to-day than formerly and the steady decline in the use of botanical drugs has further reduced the market outlet.

In this country successful commercial drug-plant culture has been limited to two periods. In the colonial days and early part of the past century herb growing as a community industry was quite profitable. Thereafter until the World War there was much experimenting but little more. The high prices during the war of many of the drugs usually imported provided an opportunity for domestic growers for several years but with the restoration of foreign supplies the new enterprises could not survive.

On the whole the situation is unchanged to-day. The same obstacles exist and the same remedies are proposed but there is no real progress toward making medicinal plant growing a staple agricultural industry in this country.

ASSOCIATION BUSINESS

AD INTERIM BUSINESS OF THE COUNCIL OF THE AMERICAN PHARMACEUTICAL ASSOCIATION, 1937–1938.

Office of the Secretary, 2215 Constitution Ave., Washington, D. C.

LETTER NO. 12.

August 13, 1938.

To the Members of the Council:

71. Committee on Requirements for Ebert and Kilmer Prizes. (See Council Letter No. 2, page 70.) Chairman M. R. Thompson forwarded the following report which has been approved by a majority of the members of the Committee, and it was thought advisable to make it available to the members of the Council for study in advance of its consideration at the meeting on August 21st:

I. EBERT PRIZE.

(*a*) *Statement of Policy.*—The Ebert Prize shall be awarded for the paper, or series of papers on the same general subject, embracing the most outstanding achievement in pharmaceutical research of any one or more years, which papers have been presented to the Program of the annual meeting of the ASSOCIATION in any one of the sections of the Program. Until a greater one is established, the Ebert Prize is to be regarded as the highest award for research achievement that it is possible for the ASSOCIATION to bestow. The award shall be made at the usual time of any year in which a sufficiently meritorious paper has been presented. If a sufficiently outstanding paper has not been presented, the award shall not be made for that particular year.

(*b*) *Ebert Prize Committee.*—The Committee shall consist of five members, one of whom shall serve as Chairman, and each of whom shall have equal voting power. The members of the Committee shall be selected in such a manner as to insure adequate representation in each of the branches of science peculiar to pharmacy, so that all papers in these different branches can be competently judged. If it is possible to avoid it, an individual who is eligible for competition in the award should not be asked to serve on the Committee. Also, whenever it is possible, the membership of the Committee should be chosen from past Ebert Prize winners.

(*c*) *General Rules to Be Followed by the Committee in Making the Award.*—All eligible papers, published or unpublished, must be reviewed by each member of the Committee. The winning paper shall be decided by the vote of the Committee. The paper receiving the majority vote shall be declared the winner and the author the recipient of the award. When a winning paper has more than one author, the award should be made to the single author who has been determined by the Committee to be responsible for the greatest or most important part in the initiation, direction and execution of the problem and in the writing of the paper.

Doctors and Masters' dissertations, or papers taken therefrom, shall be eligible for the award. If such is a winning paper, the award shall be made to the individual who was most responsible for the initiation, direction and execution of the problem embraced by the paper, whether his name appears as author or not. This is not to be construed as barring the student or recipient of the Doctor or Master's degree from eligibility in the competition. The status of the candidate or recipient of the degree shall be exactly the same, regarding eligibility, as that of possible co-authors.

Papers of past recipients of the Ebert Prize shall be given equal consideration with others in determining the winner.

When a greatly outstanding, important discovery or research achievement is reported in a paper, the Committee should exercise discretionary judgment in determining whether the award should or should not be withheld until the accuracy of the conclusions has been confirmed or substantiated by others.

Papers presented to the Scientific Section and to the sections on Historical Pharmacy and Practical Pharmacy and Dispensing containing an original investigation of a medicinal substance, chemical or pharmaceutical product or containing other original meritorious contributions in the history or sciences of Pharmacy shall be eligible for the award.

(*d*) *The Physical Character of the Ebert Prize.*—It is recommended that the medal, at present

constituting the Ebert Prize, be changed, the nature of the change to be determined by a special committee.

II. KILMER PRIZE.

(*a*) *Statement of Policy.*—Dr. Frederick B. Kilmer left a bequest under Clause 6 of his will which reads as follows: "6. I give and bequeath unto the AMERICAN PHARMACEUTICAL ASSOCIATION, organized under the District of Columbia, the sum of Three Thousand Dollars, to be held in trust, the income to be applied to the awarding of a prize for meritorious work in Pharmacognosy, such prize to be known as 'The Kilmer Prize,' or an equivalent designation. In awarding the prize preference is to be given to studies in vegetable drugs. The recipient of the prize shall be a graduate in Pharmacy. Teachers in colleges of pharmacy and workers in pharmaceutical laboratories are to be excluded from competing for the prize. Prize to be awarded under such conditions as the ASSOCIATION may elect. Funds arising from the income which may not be used are to be added to the amount of the prize or added to the principal, as the ASSOCIATION may elect."

In accordance with the provisions of this bequest, it shall be the policy of the ASSOCIATION to use the Kilmer Prize for the purpose of encouraging recent graduates in pharmacy to assume an active interest in research in Pharmacognosy.

(*b*) *Kilmer Prize Committee.*—A Committee, known as the Kilmer Prize Committee, consisting of three outstanding pharmacognosists from the membership of the ASSOCIATION shall be charged with the responsibility of naming the annual winner of this award. The Chairman of the Kilmer Prize Committee shall be further charged with the responsibility of properly announcing either through the JOURNAL or by circular to each school, early in September, that such a prize is being offered and briefly stating the rules on eligibility and other pertinent information.

(*c*) *General Rules to Be Followed by the Committee in Making the Award.*—The author of a paper on some phase of pharmacognosy, who is a member of the last graduating class, prior to the annual meeting of the ASSOCIATION, of any college or school of pharmacy, is eligible for the award. Candidates for advanced degrees are not eligible for this award.

Papers eligible for the award may be based upon either laboratory or library research. They must be written during the last year of the candidate's course in Pharmacy. The head of the Pharmacognosy Department in each school shall select the one to three best papers submitted by the graduating class of his particular school. Each school or college shall be privileged to send these papers to the Kilmer Prize Committee at the end of the school year, not later than June 1st. The Kilmer Prize Committee shall select the winner from these groups of papers submitted by the various schools of pharmacy prior to the next annual meeting of the ASSOCIATION. The winner should be notified approximately one month prior to the date of the meeting, to enable him to make plans incident to his attendance. The award shall be made during the annual meeting of the ASSOCIATION.

It shall be left to the discretion of the Kilmer Prize Committee as to whether the prize should be awarded for a given year. If the Committee finds no paper sufficiently meritorious, no award should be made for that year.

(*d*) *The Physical Character of the Kilmer Prize.*—It is recommended that the prize be made to consist of a suitable gold key, and that the difference between the cost of the key and the annual income from the bequest be awarded to the winner in cash to assist him in attending the annual meeting of the ASSOCIATION to receive the award.

72. Meeting of the Council.—Attached is the order of business of the meeting to be held on August 21st, beginning at 9:30 A.M.

73. Applicants for Membership.—The following applications, properly endorsed, accompanied with the first year's dues, and recommended by two members of the ASSOCIATION, have been received:

No. 532, Francis E. Judge, 900 Marquette, Minneapolis, Minn.; No. 533, Mark W. Judge, 800 Marquette, Minneapolis, Minn.; No. 534, Joseph Francis Greene, 1123 Pear St., Vineland, N. J.; No. 535, Harmon Carlyle McAllister, 504½ North St., Chapel Hill, N. Car.; No. 536, Mrs. Bess G. Emch, 1401 South St., Toledo, Ohio; No. 537, Joseph J. Laskarzewski, 74 S. Colony St., Meriden, Conn.; No. 538, Albert Philip Bailin, 66 Pagnuelo Ave., Montreal, Quebec, Canada; No. 539, Allyn Sumner Norton, 110 Maryland Ave., N.E., Washington, D. C.

(*Motion No. 32*) Vote on applications for membership in the ASSOCIATION. This motion will be called for at the Council meeting in Minneapolis. E. F. KELLY, *Secretary.*

PERSONAL AND NEWS ITEMS.

In the *Vienna Pharmaceutical Weekly*, **Dr. Fritz Ferchl,** of Mittenwald, has described the various German Apothecary Museums, which may be classed as follows:

Bremen, Hamburg, Hannover, Braunschweig, Düsseldorf, Eisenach, Rudolstadt, Darmstadt, Würsburg, Frankenthal, Karlsruhe, Nürnberg, Ulm, München, Wien, Innsbruck, Graz.

Special attention has been called to the outstanding features of these museums so that further strength and development can be directed. The classifications are:

No. 1: Educational subjects, exhibits and medical products. These are particularly represented in the museums at Nürnberg and München, and a large proportion date back to the 16th and 18th century.

No. 2: Department of Pharmacy.

No. 3: Refers especially to pictures, photographs and prints of the chemical industry.

No. 4: Is outstanding in the history of prominent pharmacists.

No. 5: Historical military Pharmacy.

Meyer Brothers Drug Co., St. Louis, Mo., will celebrate their 86th anniversary on September 12th. This is an enviable record, and remarkable in that the same name and same family have controlled these interests for that period of years. The firm still follows the policies established by the founder, Christian F. G. Meyer, in 1852, and its success may be attributed to giving quality first consideration and to fair and just dealings with its thousands of customers, many of whom have dealt with the house for half a century or more. There are also branches in New Orleans, La., and Little Rock, Ark.

Abbott Laboratories, North Chicago, Ill., will dedicate their new Research Building, October 7th.

The British Association for the Advancement of Science met at Cambridge University, August 18th. More than twenty-five hundred English scientists were present, also a number of notables from other countries. Among the Americans were: Dr. Robert Wood, Dr. Harlow Shapley, Dr. Herbert Ives, and Prof. Wesley C. Mitchell, president of the American Association for the Advancement of Science.

One of the most important events of the British Association's meeting will be its action on the proposal to establish a special division to coöperate with scientists of other countries in examining the social and international relations and applications of science and in defending the freedom of science and scientific workers. The council of the British Association has approved of this much-discussed project in principle, and at its Indianapolis meeting, in December of last year, the American Association authorized collaboration with the English scientists in studying the social consequences of science and resisting the attacks of totalitarian systems upon scientific thought. The position taken at the Cambridge meeting will have real importance for the public as well as for scientists.

Mr. Otto Moosbrugger, secretary of the Ohio State Pharmaceutical Association, gives an encouraging account of the recent Ohio Convention, and we are pleased to pass on to our readers some of the points of interest.

An innovation of the recent meeting was the Pioneer Ohio Pharmacists' Dinner, at which occasion sixty-eight were present, among them the Secretary of State, Wm. J. Kennedy, and former Governor George White, now a candidate for Senator from Ohio. After a fine repast reminiscences were exchanged and a more elaborate affair planned for next year. Perhaps some of our readers were confused by the word "Pioneer." The intention was to recall to younger generations the accomplishments of some of the Ohio pharmacists who introduced new practices or ideals such as Dr. Robert Ruth who pioneered and introduced National Pharmacy Week, John Uri Lloyd who developed and exploited eclectic medication to such a great extent, Dr. James H. Beal and Charles Fennel who pioneered pharmaceutical teaching, and Wahmhoff's of Delphos and vicinity, who encouraged the cultivation of medicinal drugs to such an extent that carloads of them were sent from Delphos in the proper seasons.

Among the speakers on the Program were: Dean C. L. Leonard O'Connell, "Pharmacy To-day;" J. W. Snowden, "Prescriptions Need Marketing;" Walter J. Quinlan; William J. Kennedy; C. W. Dittmer; Alexander Thomson, "Your Stake in Industry;" Thurman Miller, "Altitude," Rowland Jones, Jr., Washington Representive N. A. R. D.

Various groups of Alumni had separate dinners, in Memorial Hall were exhibits and dis-

plays visited by thousands of people, moving pictures were shown, and praise and good feeling were indulged in at the close of the Convention.

The following persons were awarded plaques for outstanding and meritorious work during the past year: L. W. Funk, Columbus; J. Otto Kohl, Cincinnati; Garrett Emch, Toledo; and Otto Moosbrugger, Dayton.

In Southern California there are four druggists on the ballot: Ray L. Riley, for U. S. Senator; James J. Boyle for Congress, 17th District; Clarence Wagner, Supervisor, 1st District; Jack Massion, for State Assembly, 66th District. All of these men understand the merchants' problems as well as those of the general public. Mr. Riley was a successful retail druggist and has had a long public career without blemish on his record. Mr. Boyle's record is so outstanding it needs no further explanation. Mr. Wagner has made a fine success both in his business and as a public servant. Mr. Massion knows our problems and can be a great help to us in our endeavor to keep business out of the racketeering class.

E. R. Squibb & Sons will organize the Squibb Institute for Medical Research, in which a staff of scientists assembled from leading institutions of the United States and foreign countries will attack problems involved in the cure of disease and relief of pain. The Institute will be housed in a new laboratory building just constructed at a cost of $750,000 in New Brunswick, N. J., and described as "the finest of its type in the world."

Dedicated to pure science, the Institute, which will be in complete operation this Fall, is the first of its kind to be founded in the pharmaceutical industry. The aim is to create in the medical and biological fields an industry-supported research enterprise comparable to the Bell Telephone and General Electric laboratories in the sphere of physics.

Men of science from all over the country will participate in the dedication of the new laboratory which will take place October 11th.

While the "First U. S. P. XI Supplement" was made up almost entirely of revised tests and assays, it is expected that the "Second Supplement," announced for January 1, 1939, will contain a number of new drugs and preparations in addition to some important revised monographs, Dr. E. Fullerton Cook, Chairman, Committee of Revision, has announced.

The American Chemical Society met in Milwaukee, September 5th to 9th. Prof. Frank C. Whitmore, Pennsylvania State College, delivered an address on "Looking Backward and Forward in American Chemistry." The Society's award in pure Chemistry was formally made to Paul Doughty Bartlett, and the Priestley Medal was presented to Marston Taylor Bogert, who delivered an address on "From the Cradle to the Grave." A number of laboratories and industrial plants were visited by those in attendance.

OBITUARY.

EDWARD H. THIESING.

Edward H. Thiesing, retired pharmacist of Cincinnati, Ohio, died August 15th, at his residence, 6320 Kincaid Road, following a long illness. He was seventy-eight years of age. Mr. Thiesing was one of the oldest living graduates of the Cincinnati College of Pharmacy. He opened his first store in 1884, in Newport. In 1895 he became owner of the store from which he retired in 1922.

Mr. Thiesing served as president of the Ohio State Pharmaceutical Association in 1917, as member of the Executive Committee of the National Association of Retail Druggists from 1910 to 1912, and as chairman of the Section on Commercial Interests of the AMERICAN PHARMACEUTICAL ASSOCIATION in 1915. He also was a director in the American Druggists' Fire Insurance Co. and an officer of the Ohio Valley Druggists' Association. At the time of his death he was Permanent Secretary of the Veteran Apothecaries Association of Cincinnati. He also was active in Masonic circles.

Surviving Mr. Thiesing are his widow, Mrs. Ottilia Schneyer Thiesing, a daughter, Mrs. Catherine Marie Clarke, and two granddaughters.

LYDIA RABINOWITSCH-KEMPNER.

Prof. Lydia Rabinowitsch-Kempner, famous bacteriologist and associate of Robert Koch in many of his most important investigations, died in Berlin, August 3rd. She was sixty-four years old. She was graduated from the Universities of Zurich and Berne, and after taking her doctor's degree, joined the Institute for Infectious Diseases at Berlin, where, under the direction of Dr. Koch, discoverer of the tubercle bacillus, she was engaged in researches of the influence of heat on bacteria and pathogenic yeast specimen.

BOOK NOTICES AND REVIEWS.

Recent Advances in Volumetric Chemical Analysis, by H. B. KELLOG, formerly Director of Laboratories, Amp. Research Laboratories, Corona, New York. 200 pages, loose leaf form, $6^3/_4'' \times 3^3/_4''$. Lefax, Inc., Philadelphia, Pa., Publishers. Price: Black faxide ring binder, $3.00; brown Castilian paper cover, $2.00.

Rapid and accurate methods are usually desired by the analyst in arriving at conclusions either in commercial or experimental work. For these reasons the author has given consideration to volumetric analysis exclusively. Most reference books give more attention to gravimetric analysis and seem to neglect rapid end-point titration methods. Carefully selected methods that have proved of practical value to the analytical and research chemist have been compiled. Sufficient details are given to enable one with an elementary knowledge of analytical procedures to follow directions. Also it offers helpful suggestions in the selections of convenient and efficient methods for rapid and accurate analysis.

The author by referring to varied sources of modern literature has brought together such applications that are more readily available for use. An added help to the analyst has been given by listing the agents necessary for each individual analysis after the method of procedure. In some cases the author has offered modification where this has been found desirable. The details differ somewhat from those given by the author originally presenting the procedure. The subject index includes: Acidimetric Indicators, Adsorption, Ceric Sulfate Solutions, New Reagents, Reductors, Acetone, Aluminum, Antimony, Arsenic, Borate, Cadmium, Calcium, Carbon Monoxide, Cerium, Chloride, Chromium, Cobalt, Copper, Cyanide, Ferricyanide, Ferrocyanide, Fluoride, Formaldehyde, Halides, Hydrogen Peroxide, Hyposulfite, Iodide, Iron, Lead, Magnesium, Manganese, Mercury, Molybdenum, Nickel, Nitrate, Nitrite, Phenol, Phosphorus, Potassium, Selenium, Silver, Sodium, Sugars, Sulfur, Tellurium, Tin, Vanadium, Zinc.

Preparation and methods of standardizing the more common solutions used in volumetric analysis are given along with the volumetric factors based on 1937 International atomic weights.—EMERSON C. BEELER.

A College Textbook of Pharmaceutical Botany (sixth edition), by H. W. YOUNGKEN, Ph.M., Ph.D., Sc.D., Professor of Botany and Pharmacognosy, Massachusetts College of Pharmacy; Member Committee of Revision, U. S. Pharmacopœia; Botanical Editor, U. S. Dispensatory, etc.

A thoroughly modern textbook with pharmaceutical and medical applications, especially adapted for students of Pharmacy and economic Botany and as a reference for pharmacists, chemists and students in structural and systematic Botany. There are chapters on: Scope and Importance of Botany; General Characteristics of Plants; The Living Cell; Life History of the Male Fern; Non-Protoplasmic Cell Contents; Plant Tissues; The Root; The Bud; The Stem; The Leaf; The Inflorescence; The Flower; The Fruit; the Seed; Classification and Naming of Plants; The Thallophytes; Fungi; Lichens; Bryophytes; Pferidophytes; Spermatophytes; Monocotyledons; Dicotyledons; Ecology; Genetics and Evolution.

The book contains 507 illustrations, Frontispiece, Glossary and Bibliography. There are 792 pages, it is bound in washable fabric, and the price is $4.75. Publishers, P. Blakiston's Son & Co., Inc., 1012 Walnut St., Philadelphia, Pa.

Chemistry of the Proteins (second edition), by DOROTHY JORDAN LLOYD, M.A., D.Sc., F.I.C., Director British Leather Manufacturers' Research Association; and Agnes Shore, B.Sc., A.I.C., Demonstrator, Physiology Department, London School of Medicine for Women. Introduction by Sir. F. G. Hopkins, O.M., D.Sc. (University of Cambridge).

The book contains a synthesis of knowledge on proteins covering every branch of science bearing upon the subject. Both the constitutional and physical phases of proteins are treated from the chemical standpoint. There are chapters on: Nature and Constitution of the Proteins; Different Classes of the Proteins; Methods of Protein Analysis; Individuality of Proteins; Biochemistry of Proteins and Amino Acids; Proteolytic Enzymes; Linkages in Protein Molecule; Architecture of Protein Molecule; Combination of Proteins with Acids and Alkalies; Properties of Protein Solutions; Absorption and Loss of Water by Gels and Tissues; Specific Effects of Salts on

Protein Solutions; Denaturation and Coagulation; Theory of Protein Solutions.

The book contains 101 illustrations; 532 pages, is bound in washable fabric, and the price is $5.50. Published by P. Blakiston's Son & Co., Inc., 1012 Walnut St., Philadelphia, Pa.

The Biological Standardization of the Vitamins, by KATHERINE H. COWARD. 227 pages. Published by William Wood & Co., Baltimore, Md. Price, $4.50.

Physiological and Clinical Chemistry, by WM. A. PEARSON and JOS. S. HEPBURN. Second Edition. 467 pages. Published by Lea and Febiger, Philadelphia, Pa. Price, $5.50.

Materia Medica, Drug Administration and Prescription Writing, by OSCAR W. BETHEA. Fifth Edition. 577 pages. Published by F. A. Davis Co., Philadelphia, Pa. Price, $5.00.

How Ancient Healing Governs Modern Therapeutics, by KLEANTHES A. LIGEROS, III. 523 pages. Published by G. P. Putnam's Sons. Price, $10.00.

Accepted Dental Remedies, by S. M. GORDON, American Dental Association Council on Dental Therapeutics. 268 pages. Published by American Dental Association, Chicago, Ill. Price, $1.00.

The Art of Dispensing, Eleventh Edition. 552 pages. Published by Chemist and Druggist, 28 Essex St., London W. C. 2, England.

Laboratory Manual for Bacteriology and Immunology, by H. D. MOOR, F. C. LAWLER and I. L. WALLACE. Third Edition. 100 pages, loose-leaf, board covers. Published by the University of Oklahoma School of Medicine, Bacteriology Department. Price, $3.50.

Gould's Medical Dictionary. Fourth Edition. 273 illustrations, 48 of which are portraits. Fabrikoid cover. 1538 pages. Price, $7.00; with thumb index, $7.50. Published by P. Blakiston's Son & Co., Inc., Philadelphia, Pa.

New and Non-Official Remedies. Descriptions of Articles Accepted by the Council on Pharmacy and Chemistry of the A. M. A. 592 pages. Published by the American Medical Association, Chicago. Price, $1.50.

Manual of Cosmetics, by CHARLES LAZAR. 318 pages. Published by The Sherwood Press, Cleveland, O. Price, $5.00.

Recent Advances in Volumetric Chemical Analysis, by H. B. KELLOG. 200 pages, loose-leaf form. Price, complete, in Black Faxide Ring Binder, $3.00; in Brown Castilian Paper Cover, $2.00. Published by Lefax, Inc., 9th & Sansom Sts., Philadelphia, Pa.

The Rockefeller Foundation, a review for 1937, by Raymond B. Fosdick.

Parenteral Therapy, by DUTTON and LAKE. 90 practical illustrations. Price, $7.50. Published by Charles C. Thomas, Springfield, Illinois; Baltimore, Maryland.

Die Rauschund Genussgifte, by PROF. DR. MED. ERICH HESSE, Pub. by Ferdinand Enke, Stuttgart.

Records of the Malaria Survey of India, published for the Indian Research Fund Association, by Thacker's Press & Directories, Ltd., Calcutta, India. Editors: G. COVELL and M. K. AFRIDI.

Qualitative Analysis for Students of Pharmacy and Medicine, by CHARLES B. JORDAN and HENRY GEORGE DEKAY. Second Edition. Published by McGraw-Hill Book Co., Inc., New York and London. Price, $2.50.

Man in a Chemical World, by A. CRESSY MORRISON. Pub. by Charles Scribner's Sons, New York and London.

Chemisch-Pharmazeutisches Bio- und Bibliographikon, by DR. FRITZ FERCHL, Mittenwald. Pub. by Arthur Nemayer, Mittenwald, Germany.

The Story of Vitamin B_1, compiled by C. R. ADDINALL, Library Service Bureau, Merck & Co., Inc., Rahway, N. J.

Introductory General Chemistry, by STUART R. BRINKLEY. 731 pages. Published by Macmillan Co., New York City. Price, $3.50.

Pharmaceutical Therapeutics, by ELDIN V. LYNN. Second Edition. 430 pages. Published by McGraw-Hill Book Co., New York City. Price, $4.00.

A Diabetic Manual, by ELLIOTT P. JOSLIN. Sixth Edition. 219 pages. Published by Lea & Febiger, Philadelphia, Pa. Price, $2.00.